ISBT International Society of Blood Transfusion

BILTEN ZA TRANSFUZIOLOGIJU BULLETIN OF TRANSFUSION MEDICINE

8. KONGRES TRANSFUZIOLOGA SRBIJE
AKREDITOVAN KAO MEĐUNARODNI
TREĆI MEĐUNARODNI KONGRES U ORGANIZACIJI UTS
29-31. OKTOBAR, 2026.
SAVA CENTAR, BEOGRAD, SRBIJA



8TH TRANSFUSION MEDICINE CONGRESS OF SERBIA
ACCREDITED AS INTERNATIONAL
3RD INTERNATIONAL CONGRESS OF TMAS
OCTOBER 29TH-31ST, 2026
SAVA CENTER, BELGRADE, SERBIA

Organizator / Organizer:
Udruzenje transfuziologa Srbije / Transfusion Medicine Association of Serbia

ZBORNIK PREDAVANJA I SAŽETAKA
LECTURES AND ABSTRACT BOOK

UDRUŽENJE TRANSFUZIOLOGA SRBIJE
TRANSFUSION MEDICINE ASSOCIATION OF SERBIA

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Poštovane koleginice i kolege, dragi gosti i partneri,

Sa velikim zadovoljstvom i izuzetnom čašću želimo da Vam uputimo najsrdačniju dobrodošlicu na 8. Kongres transfuziologa Srbije, koji je akreditovan kao međunarodni i Treći međunarodni kongres u organizaciji Udruženja transfuziologa Srbije.

Naš tradicionalni naučni skup, koji se ove godine održava od 29. do 31. oktobra 2026. godine u prestižnom ambijentu renoviranog Sava Centra u Beogradu, predstavlja ključno mesto susreta stručnjaka iz oblasti transfuzijske medicine i srodnih disciplina.

Transfuziologija se danas razvija brže nego ikada, donoseći nove standarde, tehnologije i izazove u svakodnevnoj praksi. Ovaj kongres je jedinstvena prilika da kroz bogat naučni program, plenarna predavanja vrhunskih domaćih i inostranih stručnjaka, usmene prezentacije i poster sesije, razmenimo dragocena znanja i iskustva. Naš cilj je da kroz dijalog unapredimo bezbednost pacijenata, efikasnost hemoterapije i primenu savremenih principa u lečenju krvi i krvnim komponentama.

Posebno nas raduje činjenica da kongres svaki put okuplja sve veći broj lekara i saradnika, ali i medicinskih tehničara i transfuzista bez čijeg rada i posvećenosti naš sistem ne bi mogao da funkcioniše. Vaše aktivno učešće i naučni radovi ključni su pokretač razvoja naše struke u regionu i šire.

Pored naučnog i stručnog dela, nadamo se da će vam boravak u Beogradu pružiti priliku za obnavljanje starih i uspostavljanje novih profesionalnih i prijateljskih veza koje čine srž našeg udruženja.

Želimo vam uspešan rad, inspirativne diskusije i prijatan boravak na Kongresu!

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Predsednik Naučnog odbora

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Dear colleagues, dear guests and partners,

It is with great pleasure and immense honor that we extend our warmest welcome to the 8th Congress of Transfusion Medicine of Serbia, accredited as an international congress and recognized as the 3rd International Congress organized by the Association of Transfusion Medicine of Serbia.

Our traditional scientific gathering, which will be held this year from October 29 to 31, 2026, in the prestigious setting of the newly renovated Sava Centar in Belgrade, represents a key meeting point for experts in transfusion medicine and related disciplines.

Transfusion medicine is developing faster than ever, bringing new standards, technologies, and challenges to everyday clinical practice. This congress offers a unique opportunity to exchange valuable knowledge and experience through a rich scientific program featuring plenary lectures by leading national and international experts, oral presentations, and poster sessions. Our goal is to advance patient safety, the efficacy of hemotherapy, and the implementation of contemporary principles in the treatment and management of blood and blood components through dialogue and collaboration.

We are particularly pleased that the congress continues to bring together an ever-growing number of physicians and other healthcare professionals, as well as medical technicians and transfusion specialists, without whose dedication and commitment our system could not function. Your active participation and scientific contributions are essential drivers of the development of our profession, both in the region and beyond.

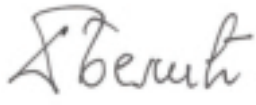
In addition to the scientific and professional program, we hope that your stay in Belgrade will provide an opportunity to renew longstanding relationships and establish new professional and personal connections that form the very heart of our association.

We wish you a successful congress, inspiring discussions, and a pleasant stay!

We look forward to welcoming you to Belgrade.



Ana Momčilović
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8. KONGRES
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CLINIC-BASED DESIGNS, DATA AND EXPERIENCES HELP / ENHANCE THERAPEUTIC APHERESIS

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Abstract

Apheresis could be defined as an effective and "easy-to-use" hemomodulatory system with the goals of : 1) harvesting of blood components – cells, plasma or plasma constituents – from donor's blood (apheretic donation – AphD) and 2) removal of some "pathogenic agent" or "disease-causing entity/factor" (which is in fact never a living microorganism – "non-microbial" etiopathogenesis) or reducing of excessive/abnormal constituents from patient's bloodstream (therapeutic apheresis – TAph) – followed by positive 3 effect.

Based upon the criterion of what is the removed blood constituent or apheresis substrate – it is possible to classify TAph into "conventional" or "standard" (versus "selective") therapeutic plasma exchange (TPE) and therapeutic cytapheresis (TC) procedures. Standard TPE providing rapid removal of plasma (one or more patent's circulating volume) regardless of which fluid – colloids, crystalloids and allogeneic or immunoadsorbed autologous plasma – is used as a replacement. TC procedures, combined with immunomodulating drugs and other medical support, result in hemobiological and patient's clinical recovery. The purpose of conventional TC is to reduce excessive cellular count (cytoreduction) in circulation or body and to alleviate symptoms produced by excess of these cells.

The purpose of this paper is to provide a short overview of recent knowledge regarding apheresis (primarily TAph) techniques and to summarize evidence-based practical apheretic approaches with brief presentation of our own result using different apheresis treatments.

Key words: apheresis, therapeutic plasma exchange, leukapheresis, plateletapheresis, erythrocytapheresis

Sažetak

Aferezu je moguće definisati kao efikasan i "za upotrebu jednostavan" hemomodulacijski sistem čije su osnovne namene: 1) prikupljanje krvnih komponenti – ćelija, plazme ili sastojaka plazme – iz krvi donora (aferezna donacija – AphD) i 2) uklanjanje nekog "patogenog agensa", odnosno "entiteta/faktora uzročnika bolesti" – koji zapravo nikada nije živi mikroorganizam ("ne-mikrobna" etiopatogeneza) ili redukcija prekomernih/abnormalnih sastojaka iz krvotoka bolesnika (terapiska afereza – TAph) – praćena pozitivnim kliničkim efektom.

Na osnovu kriterijuma šta je uklonjeni sastojak krvi ili supstrat afereze – moguće je klasifikovati TAph u "konvencionalnu" ili "standardnu" (versus "selectivnu") terapijsku izmenu plazme (TIP) i terapiske citafereze (TC). Standardna TIP omogućava brzo uklanjanje plazme (minimum jedan cirkulišući volumen) bez obzira na to koja se tečnost – koloidi, kristaloidi, odnosno alogena ili imunoadsorbovana autologna plazma – koristi kao nadoknadna tečnost. TC procedure, u kombinaciji sa imunomodulacijskim lekovima i drugom medikacijom, rezultuju hemobiološkim i opštim oporavkom bolesnika. Cilj konvencionalne TC je redukcija prekomernog broja ćelija (citoredukcija) u cirkulaciji ili telu i ublažavanje simptoma izazvanih viškom ovih ćelija.

Osnovni cilj ovog rada je da pruži kratak pregled aktuelnih saznanja o tehnikama afereze (prvenstveno TAph) i da sumira praktične aferezne pristupe zasnovane na dokazima, uz kratak prikaz sopstvenih rezultata korišćenjem različitih afereznih tretmana.

Ključne reči: afereza, terapijska plazmafereza, leukafereza, trombocitafereza, eritrocitafereza

Introduction

The word apheresis derived from Greek phrase *aphaíresis* (ἀφαίρεσις) or *apheresis*, as well as from Latin term *aphaeresis* (also spelled *apheresis*) meaning "taking away" or "to withdraw" (1, 2). Apheresis could be characterized as an extracorporeal blood separation and purification technology, as well as an effective hemomodulatory system. From the medical viewpoint, these procedures are useful for plasma/cell collection from bloodstream of healthy persons' (apheresis donation – AphD). Therapeutic apheresis (TAph) includes exfusion (transitory removal) of the part of whole blood, its *ex vivo* processing (separation) into plasma and cells, elimination of altered/abnormal or quantitatively changed (excessive) constituent(s) – followed by returning of the "rest" (remaining blood fraction) into the patient's circulation. Blood cells or plasma can be replaced with normal cells, plasma or an appropriate replacement fluid. The goal of TAph is to reduce the level of "disease-causing" circulating agents – directly or indirectly responsible for etiology and the "step-by-step" development (pathogenesis) of disorders – to the stage that will allow improvement and patient's clinical recovery. Typically, TAph should be combined with immunomodulating medication and other (palliative) drug administration (3–8).

A more recent categorization of apheresis includes classification into AphD, TAph and so-called diagnostic apheresis (DgAph) procedures. The last one consist of the following actions: exfus ion of patient's blood, its separation into components and *ex vivo* concentration of some specific "minor-level" constituent(s) due to superior identifying (diagnosis) and determining of disease characteristics (for example, hematology and cancer research), as well as seldom to predict its course or patient survival (2).

Based on type of apheresis substrate, procedures can be classified into plasmapheresis and cell harvesting (cytapheresis) in AphD setting, as well as therapeutic plasma exchange (TPE) and therapeutic cytapheresis (TC) in TAph setting (5–13). When relatively small quantity of plasma is separated from whole blood – without infusing any replacement fluid or sometimes infusing only saline ≤ 500 mL – plasmapheresis is the appropriate term for this procedure (5, 6). Thus, using plasmapheresis (AphD procedure) relatively minor quantity of plasma (typically 500–600 mL or less than 15% of total circulating blood volume) is collected from bloodstream of healthy person (donor). The purpose of cellular AphD-practice is to collect hematopoietic stem cells (SCs) and mature blood cells with high "target-cell" quantity and quality in the harvest (6–8, 12, 13).

AphD procedures will not be described in this paper. In the next part of the manuscript, the categories TAph, mechanisms of their therapeutic action, indications and clinical effects will be briefly illustrated – with a summarizing of clinical outcome in our patients.

Therapeutic apheresis – general and methodical consideration

The most frequently applied TAph procedure is "conventional" or "standard" TPE. It is a curative apheretic technique in which part of patient's blood is passed through specific equipment (cell separator or rarely filtration sets) to separate plasma from cellular components. The plasma is then removed (one or more circulating volume) and replaced by an adequate substitution fluid – with suitable oncotic effect, non-toxicity and biological tolerability. Then the remaining (or modified) part of the blood needs to return into the bloodstream of patient. Thus, standard TPE is when providers (qualified medical personnel) use plasmapheresis to replace the part of patient's plasma (3–6).

Natural or biological colloids (for example: 5% albumin) and a combination of crystalloids (for example saline) with colloid solutions are most often used as replacement fluids. Occasionally, for substitution of removed plasma allogeneic plasma or cryosupernatant (example: treatment of thrombotic thrombocytopenic purpura – TTP) or immunoadsorbed autologous plasma (example: the use of selective TPE) can be utilized (5–7, 14–17).

The main disadvantage ("weak point") of standard TPE is the absence of "depletion selectivity". However, nowadays various innovative selective TAph techniques are known – such as system for TPE with extracorporeal immunoadsorption (TPE-ECIA), double-filtration-plasmapheresis (DFPP), rheopheresis, adsorptive cytapheresis and extracorporeal photopheresis (ECP) (3–6, 14–17).

The use of TPE-ECIA system selectively reduces of injuring ("disease-causing") agents or "disadvantageous" or "potentially harmful/destructive" plasma constituents (alloantibodies before ABO-incompatible stem cell – SC or organ transplants), while the functional component(s) – like albumin, coagulation factors and beneficial or necessary immunomodulating compound – are returned to the bloodstream. Thus, the use of TPE-ECIA system guarantees high degree of blood purification with low risk of normal plasma component loss and inferior rate of adverse events – both acute and delayed (immunomodulation and/or virus transmission) since the removed plasma by immunoadsorbed autologous plasma is substituted (4, 14–17).

The standard TC is an effective and "rapidly-acting" disease-modifying curative method for "redesign" of blood cell "over-production" – which can efficiently prevent the occurrence of "cytemias-related/induced" adverse events. Using TC procedures, altered cells (in terms of total cellular mass or their quality) are removed from patient's blood and/or replaced with normal cells (for example, red blood cell exchange – RBCX). The aim of standard TC is to decrease excessive cellular count through "cytoreductive" effect and to improve and/or alleviate symptoms produced by different cytemias, that is with "over-counted" cellular component(s) (1–3, 9–11).

According to cells removed, TCs can be classified into subsequent procedures: 1) therapeutic leukapheresis (TL); 2) therapeutic thrombocytapheresis or plateletapheresis (TP); 3) therapeutic erythrocytapheresis (TE) and RBCX (3–6, 9). The goal of specific or selective TCs – such as ECP, adsorptive cytapheresis (granulocyte or monocyte reduction) – is both blood cell counts decrease and "disease-responsible" cell(s) *ex vivo* modification or replacement (exchange) (3–7).

By TL patient's blood is passed through cell separator, which isolates and removes selected white blood cells (WBC) – mainly leukemic blasts – and returns the remainder of the patient's circulation, with or without addition of replacement fluid. The aim of TLs is WBC count reduction and reverse of the "hyperleukocytosis-leukostasis" syndrome, regression of lymphadenomegaly and improvement in general clinical status. The TL procedure represents a rapid "cytoreductive" treatment of "leukostasis crisis" when the number of circulating WBC $\geq 150x10^9$/L. The apheretic treatment of patients with very high WBC number ($\geq 500x10^9$/L), their removal by TL would have been adequate to "partial excision" of tumor mass even 1,000 – 1,500 g of "total-cell-mass" in eliminated apheresis product (3–5, 10, 11).

TP is an apheretic procedure in which blood of patient is passed through a medical device which separates/removes the excess of platelets (Plts) and returns the remainder of the patient's blood – typically without addition of any replacement fluid. The TPs are useful in the treatment of patients with thrombocythemia and symptomatic thrombocytosis (Plt $\geq 1,500x10^9$/L) until chemotherapy, antiplatelet drugs and other medication takes effect. The reason for TP might be determined as a method for rapid reestablish of Plt "over-production" followed by prevention of "thrombo-hemorrhagic" events (thromboembolism is more frequent than bleeding crisis). The arterial thromboses (resulted by cerebrovascular, coronary or other occlusive episodes) happen more often than venous events (3–5, 9).

The aim of TE treatment is to obtain hemorheological advances – that is to manage cellular hyperviscosity by rapid reduction of high hematocrit (Hct) with following prevention of vaso-occlusive complications and potential organ damages. Beside removal of the excess of red blood cells (RBCs) from patient's circulation, with TE it is possible to achieve hematological and hemorheological recovery with consecutive improvement of tissue perfusion and oxygenation. The target Hct ≤ 0.45 % is for patients with polycythemia vera (myeloproliferative neoplasm), Hct between 0.50 and 0.52 is for patients with pulmonary hypoxia or high oxygen affinity hemoglobin and target Hct values 0.55 – 0.60 are for patients with cyanotic congenital heart disease. The reason for RBCX is a replacement of altered RBCs and correction of anemia, with consecutive frequently long-term beneficial effects. The patient's RBCs are removed and replaced with donors' cells and colloid solution (3–7, 10, 11).

Among selective or specific cytaphereses, the adsorptive TC (granulocytapheresis) and ECP should be mentioned. The first one represents therapeutic procedure in which blood of the patient is passed through a cell separator system, which contains an additional column or filter that selectively adsorbs activated monocytes and granulocytes, allowing the remaining WBCs and other blood components to be returned to the patient (3–5, 11) Briefly, ECP is therapeutic procedure in which the buffy coat is separated from the patient's whole blood, treated *ex vivo* (extracorporeally) by some photoactive compound (for example, psoralen) and exposed to ultraviolet A (UVA) light then subsequently reinfused to the patient during the same procedure (3–5).

Commonly, TCs performed by cell separators operates in a fully automatic manner, thus enabling intra-apheretic cell recruitment and minimizing manual alterations or inter-individual variations.

The idea of our original "multi-manner" or "multi-modal" therapeutic apheresis (MMAph) – altering at the same time more than one blood component(s) – is to create an option for rapid (through one to three hours) returning from some life-threatening "irreversible" emergency to the "district" of reversible (although yet imbalanced) clinical crisis with highly probable positive outcome and recovery of the patient's blood homeostasis, as well as overall clinical response (5, 18–20).

Finally, it is important to highlight that TAph is an aggressive therapeutic method, by which there is direct intervention within the patient's circulation and therefore, it might be followed by adverse events and side effects. To minimize them, special criteria for choice of apheretic donors and patients must be applied (7, 10). The performance of TAph is not possible without good understanding elementary data related to physiology, hemorheology, disturbances in the bloodstream and cardiopulmonary reanimation. Finally, the condition for successful performance of apheresis is also laying in proficiency of the team members for the work with extracorporeal circulation and manipulation with entire modern equipment (5, 10).

Therapeutic apheresis – our clinical studies and data

In our institute, TPE has been introduced already in 1966 (using plasmapheresis sets) for therapy of multiple myeloma with serum hyperviscosity syndrome and subsequently in 1979 (by cell separator) for treatment of different immune-mediated neurological disorders (IMNDs) (10).

Our clinical studies – based on more than half century decades experience with apheresis – confirmed that treatment by TPE gave the best therapeutic response in patients with TTP and IMNDs – i.e. myasthenia gravis (MG) and acute inflammatory demyelinating polyradiculoneuropathy (APRN) or Guillain-Barre's syndrome (22, 23). The use of TPE was also useful in the therapy of Goodpasture's syndrome, some exogenous poisoning, glycogenosis type 1 associated hyperlipidemia, cryoglobulinemia with polyneuropathy, hypersensitivity vasculitis and other disorders (5, 10, 21–23).

Namely, performing TPE undoubtedly positive clinical response was obtained in patients with TTP (laboratory and clinical remission). The number of applied TPEs in the treatment of a young female patient was the highest (35 procedures) and the total volume of the removed total plasma volume was 101.6 L (replaced by 76 L cryosupernatant and the rest with saline). Patient tolerated well the intensive TPE–treatment without adverse effects (22).

TPE used TPE for serum hyperviscosity syndrome resulted in reduction of plasma paraprotein level, significant hyperviscosity reduction and clinical improvement. There were beneficial therapeutic effects of TPE also in patients with circulating immune complexes. The use of TPE in the treatment of cryoglobulinemia resulted in a decrease in cryoglobulin concentration followed by improvement in renal function and other abnormalities. Patients with cold agglutinin disease had better laboratory findings and good clinical improvement (5, 22).

In the therapy od IMNDs, anti-inflammatory and immunosuppressive medication (used simultaneously/synchronously with TPE) should inhibit a "rebound" increase of (auto)antibody synthesis. TPE can also be effective when antibody is not demonstrable, suggesting that current assays do not detect all pathogenic antibodies and other "immune reactants" (5, 10, 23).

In patients with MG improvement was manifested with recovery of the rough motor activity, disappearance of respiratory failure, improved speech, normalization of the chewing and swallowing functions and disappearance of visual problems. If the "MG-crisis" was recurred or patient's condition was aggravated, TPEs were repeated. Finally, for a few MG patients, TPE procedures were performed intermittently once monthly. The results obtained for APRN confirmed that there were significantly better and faster improvements and recoveries from neurological deficiency and peripheral nerve conduction in patients treated with a combination of immunosuppressive drugs and TPE – particularly when TPE started early in the course of the disease (5, 22, 23).

The basic goal of our original TPE-ECIA treatment was to reduce the circulating (allo)antibody level to less than the "critical-threshold" (an acceptable titer ≤ 8) immediately prior to taking patient to ABO-incompatible kidney transplant (16, 17).

In preclinical research (16), the efficacy of our original "pre-conditioning regimen" – using ECIA-based "closed-circuit" system – for ABO-incompatible kidney transplants was evaluated. As confirmed, parameters of biochemistry, hemostatic activity, immunoglobulin and complement levels were practically identical in plasma samples before and after ECIA. Opposite, donor-specific ABO alloantibody concentrations in recipient plasma were significantly reduced (5, 16).

It was also presented that the use of our own preconditioning regimen – including anti–CD20 infusion, TPE-ECIA and standard immunosuppression – resulted in high anti-A/B reduction before kidney transplant (target antibody titer ≤ 4) with positive peri-transplant multi-laboratory findings and overall clinical outcome of transplants (17).

Thus, it was confirmed that the use of anti-CD20 and our original TPE-ECIA system with triple immunosuppression resulted in rapid ABO-antibody depletion and beneficial clinical results. There were neither side effects of apheresis, nor any intraoperative complications or graft rejection [5, 17].

Using TE, the most important positive effects were reduction of cellular hyperviscosity syndrome with consecutive regression of symptoms caused by elevated blood viscosity, resulting in better microcirculation and tissue perfusion. In our apheresis center, RBCX procedure were successfully performed for the treatment of malaria ("parasitized-RBC" ratio was up to 70%) and hemolytic crisis in DAT and IAT positive severe autoimmune Hemolytic Anemia (AIHA) for replacement of altered or damaged cells with normal RBCs. RBCX – combined with TPE and standard immunochemotherapy – resulted in blood purification (TPE effect), correction of anemia and long-term beneficial clinical effects. The main goal was to replace antibody-coated (i.e. altered/damaged) RBCs and to prevent further "cytolysis-related" anemia and complications (5, 11, 19).

Our experience has shown that the use of TL, as an initial therapy in hyperleukocytosis leukocytosis, resulted in a high-quality cytoreduction. Typically, TP treatment was used when the Plt number ≥ 1,500x10^9/L ("hyper thrombocytosis" or "extreme thrombocytosis" – ETC), although the degree of thrombocytosis and the complexity of clinical status are not always causally linked. TP treatment by rapid cytoreduction and decreased occurrence of thrombotic-hemorrhagic events were associated (5, 9–11, 24).

The use of MMAph in our patients resulted in: 1) rapid and intensive recovery of blood oxygen-carrying capacity (without circulation overload); 2) optimization of plasma and total body fluid volume and 3) hemorheological repair. Thus, beneficial effects of MMAph were coming from the removal of unwanted agents from circulation and/or extensive enrichment of deficient blood component(s) – without excess of intravascular volume (5, 18–20).

Conclusion

Clear evidence of the beneficial effects of conventional or standard TPE in the treatment of immune-mediated hematological and neurological diseases/disorders was demonstrated. TPE might limit damage to various organs, accelerate recovery and result in the improvement of patient's general clinical status. Our clinical studies confirmed that neither TL nor TP resulted with a long-term clinical benefit in acute leukemias or essential thrombocythemia, despite of transient decrease in circulating WBC and Plt counts. Even more important is the fact that TC procedures never altered basic hematopoietic abnormality and they were never associated with bone marrow remission

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ACCREDITATION IN ASIAN COUNTRIES: IMPROVING QUALITY IN NATIONAL BLOOD TRANSFUSION SERVICES

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Abstract:

Accreditation is a voluntary process. However, it is an important process in quality management system which is being certified/ accredited by an external agency. Accreditation is a higher platform in quality management system. There are accreditation agencies at national or international level in Asia and they offer accreditation on the basis of their respective Standards. Standards for blood bank accreditation is usually based of ISO-15189. Asian Association of Transfusion Medicine (AATM) usually operates in greater Asian region and it has 26 member countries in this region. AATM member countries usually have the opportunity to go for AABB accreditation, AABB Quality certificate, NABH accreditation or national accreditation exist in individual countries. AATM advocates for AABB Quality Certificate which was specifically crafted for AATM member countries on the basis of AABB Fundamental Standards. It is already been adopted in four Asian countries and more Asian countries are going for this program. Few AATM member countries also have adopted AABB accreditation. In six countries from Indian peninsula, have gone for NABH accreditation. Therefore, AATM member countries have multiple choices to go for quality improvements including accreditations.

Keywords: Blood Bank, accreditation, quality management system

Introduction

Blood transfusion service is a vital part of the health care service in a country. A well-organized blood transfusion service, with quality systems in all areas, is a pre-requisite for the safe and effective use of blood and blood products at every blood banks in the country. The quality implementation should be uniform in all blood banks. An integrated strategy for blood safety is required for elimination of transfusion transmitted infections (TTI) and for provision of safe and adequate blood supply to the people. Increasing technical advancement in the field of Transfusion Medicine has necessitated enforcing measures to ensure quality of blood and its products. The blood transfusion system has made significant advancements in areas of donor management, storage of blood, grouping and cross matching, testing for transmissible diseases, rationale use of blood and distribution etc. in last decade. For quality, safety and efficacy of blood and blood products, well-equipped blood centres with adequate infrastructure and trained manpower are an essential requirement. For effective clinical use of blood, it is necessary to train clinical staff. To attain maximum safety, the requirements of good laboratory practices (GLP), good manufacturing practices (GMP) and moving towards total quality management are vital for organization and management of blood transfusion services (1).

Accreditation of a blood bank or a blood transfusion service is voluntary quality assurance process based on strict adherence on an operational safety Standard. This Standard may be different on international Standard following by respective organizations. This Standard ensures compliances on quality of blood collection, testing, processing, issuing and distribution maintaining cold chain whenever applicable. Accreditation clauses not only cover process control and also other processes involved in the blood bank including infrastructure, procurements, human resources management, documentation etc.

However, Good Manufacturing Practices (GMP) is that part of quality assurance which ensures that products are consistently produced and controlled appropriately to their intended use, as per the defined standards. In 1963, USFDA developed GMP regulations for pharmaceutical industries. USFDA enforced GMP in Blood Transfusion Services (BTS) because of inadequate documentation. Thereafter UK regulators also developed GMP guidelines in Blood Transfusion Services. In 1992 European Councils enacted rules for Medicinal products. Implementation of GMP in BTS is difficult because of batch variation, and unlike pharmaceutical industry all the batches do not undergo quality check.

Need for accreditation:

Why is there a need for Blood Bank/ Blood Transfusion Services (BTS) accreditations? Blood Bank/ BTS accreditation results in high quality of patient care with supply of safe blood to the right patient in right time and right quantities. Accreditation for Blood Banks/ BTS conforms to the highest international standards usually on the basis of ISO-15189. Accreditation gives definite advantages to blood bank/ BTS for developing confidence for patients visiting hospitals/ blood banks for any treatment/ requirements. Accreditation improves the quality standards of a blood bank/ BTS in all areas of collections, processing, testing, compatibility, transfusions, hemovigilance and quality assurances. Due to high quality standards, biggest beneficiaries of accreditation process are all patients, blood/ component donors and clinicians. Efficiencies and competencies of blood banks and BTS staff have improved significantly and benefits are enjoyed by clients. Community confidence improves and public is assured of obtaining safe and quality blood and components from accredited blood banks. Staff of accredited blood bank/ BTS are continuously kept updated with knowledge and competencies in systematic ways with defined ownerships and accountabilities. Accreditation process ensures enforcement of complete enforcement of regulatory processes and national/ international guidelines (2).

Various accrediting agencies: There are few accrediting agencies managing accreditation program globally on blood banks/ blood transfusion services or laboratory services. Out of them, following accreditation agencies are working in different parts of the world.

Association for the Advancement of Blood & Biotherapies (AABB, Accreditation): This is one of the oldest/ long standing accreditation programs and it is considered as a gold standards for transfusion services and full process control of blood banking. This accreditation is done on the basis of AABB Standards.

Association for the Advancement of Blood & Biotherapies (AABB, Quality Certificate): This is a certificate program organized by AABB on the basis of their Fundamental Standards. This program is desk top assessment and mainly aimed for blood bank/ transfusion services of low and medium income countries (LMIC).

Africa Society for Blood Transfusion, Stepwise accreditation: Offers accreditation programs for blood transfusion activities across the African continent. It is available in first two steps in certification followed by 3rd step as full accreditation.

National Accreditation Board for Hospitals & Healthcare Providers (NABH): This program is being managed under the Quality Council of India (QCI) and primarily focused on 11 healthcare verticals. It includes hospitals, blood banks, medical imaging services, eye care organizations etc. NABH also extended its accreditation programs to six other countries.

National Accreditation Board for Testing and Calibration Laboratories: This Board is under QCI and deals with accreditation testing and calibrating laboratories, mainly in India

College of American Pathologists (CAP): Provides accreditation for clinical laboratories, including transfusion services, to ensure high standards of testing accuracy and patient safety.

There are few basic elements for blood bank accreditation. Following is building blocks in accreditation system to cover all quality parameters in a blood bank/ blood transfusion services (2).

- Quality management
- Personnel and organization
- Premises, equipment and material
- Documentation
- Collection, testing and blood processing
- QC and proficiency test
- Complaints & component recall
- Investigation of errors and accidents rejected units disposal and sample retention
- Self assessment, internal and external audit

1. Quality management

It starts with quality management of the blood centre. Management commitment is the utmost important to implement quality standards. Quality is the responsibility of all people/ staff working in blood centre (2, 3). There should be separate quality assurance departments reporting directly to Medical Director or In-charge blood centre. QA department should have designated Quality Manager, Quality Control (QC) and Qualified Person (QP). Qualified person is the designated individual who has the authority to release blood components/ product for the use of patients. Another norm of GMP is that the production department head should be separated from QA department so that QA can function without any bias.

2. Personnel and organization

The Organogram should clearly define the reporting system of the institute/ organization. Blood bank should have adequately trained staffed for smooth functioning. Job description and key results should be defined for all the staff. Only qualified and trained personnel should be appointed to work in blood bank. When new person is recruited, he/she should undergo induction program and proper training of work is to be done. Continuous in-service training is also important. All training programs should include the concept of quality so that everybody is aware about the principles of GMP (2).

3. Premises, equipment and materials

Premises:

Blood bank premises should be planned and constructed for maintaining The premise should be designed with the aim to minimize the errors and functions can be carried out in orderly manner. Certain areas like quarantine require special attention; quarantine area should be lockable. Similarly, storage area must be temperature controlled, monitored and checked regularly (3).

Equipment

All equipment in the laboratories should be adequately planned and placed for optimum functions. Equipment should be installed and validated as per design before it is being taken into use (1). Proper preventive measures are important like warranty or annual or comprehensive maintenance contract (AMC/ CMC). Regular calibration should be carried out for all equipment. Validation and calibration should be documented (3). Equipment logbook should be maintained for all critical equipment.

Material

Before purchase of material specifications should be defined as per the working system, workload and infrastructure of BTS. Material should be purchased from qualified vendors only (1). At the time of receiving material pre-receipt checks should be done. If any deviation is found, manufacturer should be informed. The material received should be released by authorized people only, and FIFO should be follow.

4. Documentation

Documentation is important aspect of QA. Documentation ensures that work is standardized and there is traceability in all steps in manufacturing process (2). There are different levels of documentation. First level is comprised of Quality Policies and Quality Manual; second level is procedures, processes, and process control. Third level documents are SOPs. Fourth level documents are various records, forms, labels, registers, data sheets etc. The corrective loop of documentation system defines the required standards and also ensures the standards are followed also. This will also help to identify the steps which require revision or correction.

The corrective loop includes the basic principles of

“write what you do”
↓
“do what is written”
↓
“record what you did”
↓
“revise what you will be”

All the documents should be signed with date and time.

Records are working documents that are completed or generated during a work activity. All the records are stored for the defined period (as per law) (3). Records can be preserved in form of hard copy, soft copy, microfilm etc. If data are recorded and stored in computers, it is necessary that the software in use have passed through validation process (1). There should be different levels of security to maintain confidentiality and to avoid tendering of data.

5. Collection, testing, blood processing

Final product depends on raw material. All the process should be carefully defined and controlled. System traceability is must. For collection and processing of blood components the collection container should be sterile and closed to avoid any contamination. All the containers should be labeled for collection date, unique identification number, expiry date, results of screening test, blood group etc. Once the blood is collected it should be stored and transported at required temperature. All the

component storage cabinets should be provided with continuous temperature monitoring system with alarm. The blood center should have power back up system to take care of power failure. Testing results should be validated by supervisor. Regular QC of components and reagents should be done on regular basis. If any deviation is found, actions should be taken to find out reason for deviation and corrective action should be taken (3).

6. QC & Proficiency testing

Proficiency testing is one means for determining that test systems (including methods, supplies, and equipment) are performing as expected (1). QC activities including steps of verifications & testing which are used to assured that material & process meet their specification. Internal QC following lab procedure by using QC samples & all procedures to correct & prohibit deviations. External QC is the analysis of unknown samples & evaluation by 3rd party. Proficiency testing ability of personnel to perform tasks they are supposed to do.

7. Complaints and component recall

There should be a system of grievance handling and feedback to the customer (donor and patient/doctors). Donors should be informed about their TTI status after blood donation (2). Similarly for blood components also system should be place to recall the component and to inform hospital or treating doctor. Hemovigilance/ biovigilance / look back system is an important aspect of QA. All the processes if documented as per system will support to have traceability of each donation right up to its final issue to the recipient.

8. Investigation of errors and accidents

Error management system will help to register errors and accidents and to identify the system problems. Well defined error management system will help to find causes of errors so that corrective action can also be defined for future. Priorities should be given to investigations of incidents with potential risk for serious adverse events. All the adverse incidents should be documented.

9. Sample retention & disposal of units

Blood samples of patients should be preserved for as per rules and SOP of the blood center. Patient's samples should be preserved for 7 days, donor samples for 30 days or 5 years as per regulatory norms in respective countries. Disposal of rejected units, low volume, biohazardous units etc. should be disposed of as per SOP and as per national regulations with traceability (2).

11. Internal and external audits

Internal audit requires monitoring & document compliance of GMP/ISO and to propose necessary corrective action. These are internal process to assess the quality systems of BTS. [3] All audits must be documented and recorded.

Phases of GMP:

Implementation of GMP is a challenging job. This process can be divided into three phases. In phase I, it is very important to take commitment of management and to train all personnel of the BTS. Proper training and involvement at all levels is the driving force at initial phase. In Phase II, GMP applications are carried out at different levels. It includes application in manufacturing processes, preparation of flow charts, process validation, calibration and validation of equipment, validation of kits and reagents. In the third phase, it is continuous monitoring, error prevention, corrective actions and continuous improvement with proper vigilance.

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PEDIATRIC THROMBOSIS IN THE CONTEXT OF DEVELOPMENTAL HEMOSTASIS: A GENERAL REVIEW

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Abstract

Developmental hemostasis describes the age-dependent evolution of the coagulation system from fetal life through adolescence, fundamentally distinguishing pediatric from adult hemostasis. Although venous thromboembolism (VTE) is uncommon in the general pediatric population, its incidence rises dramatically among hospitalized children and neonates, particularly with central venous catheters, malignancy, and congenital heart disease. Two incidence peaks occur: the neonatal period and adolescence. Accurate diagnosis requires age-specific reference ranges, as the hemostatic system develops with age. Proteomic studies from our group have revealed age-specific differences in plasma proteins, fibrinogen structure, and heparin-binding proteins, providing molecular insights into hemostatic proteins in healthy children. Treatment for pediatric thrombosis is rapidly evolving, with direct oral anticoagulants (e.g., rivaroxaban and dabigatran) approved for pediatric use and endorsed by 2024 international guidelines. Future research should leverage multi-omics approaches (e.g., proteomics, genomics, and transcriptomics) to comprehensively map the molecular landscape of developmental hemostasis and identify novel biomarkers and therapeutic targets for pediatric thrombosis.

Keywords: developmental hemostasis; pediatric thrombosis; age-specific differences

Introduction

The incidence of pediatric venous thromboembolism (VTE) has risen significantly over the past three decades, driven by advances in supportive care, expanded use of central venous catheters (CVCs), increasing survival of children with chronic conditions, and improved diagnostic sensitivity. Hospital-acquired pediatric VTE in the United States alone has increased by more than 130% between 2008 and 2019, rising from 46 to 106 cases per 10,000 hospitalizations (1).

Understanding pediatric thrombosis requires appreciation of developmental hemostasis, the dynamic, age-specific evolution of the coagulation system from birth through adolescence, first described by Andrew and colleagues in the late 1980s (2). My research has extended this concept to the molecular level, demonstrating age-specific differences in plasma proteins, fibrinogen structure, and heparin-binding interactions that explain the age-specific development of the hemostatic system across increasing age in healthy children (3–5).

This review synthesizes current evidence on the epidemiology, pathophysiology, diagnosis, and treatment of pediatric thrombosis within the developmental hemostasis framework, and highlights how multi-omics methodologies may transform future understanding and management in this setting.

Developmental hemostasis: concepts and clinical implications

Andrew et al. established that at birth, vitamin K-dependent coagulation factors (II, VII, IX, X) and contact factors (XI, XII) are markedly reduced relative to adult values, while von Willebrand factor (VWF) is elevated and enriched with ultra-large multimers enhancing platelet adhesion (2). Natural anticoagulants, protein C, protein S, and antithrombin, are also reduced in neonates compared to adults, yet the overall procoagulant–anticoagulant equilibrium is maintained, protecting neonates from hemorrhage and thrombosis under physiological conditions.

My research has characterized these age-specific differences at the molecular level. We demonstrated that fibrinogen

in neonates and children differs structurally from adult fibrinogen: the Aα chain is consistently higher in molecular weight by up to 1,500 Da, reflecting age-specific posttranslational modifications that may confer thromboprotection in early life (4). We initially identified significant differences in up to 100 protein spots across age groups spanning neonates to adults, encompassing proteins involved in hemostasis, iron transport, and immune response (3). This work was followed by more modern quantitative mass spectrometry which further established a normative proteomic atlas across neonates, children, and adults, confirming that age-specific variability is pervasive across the plasma proteome (6).

We also investigated the mechanistic basis for age-related differences in heparin pharmacodynamics, revealing that the total number and concentration of heparin-binding proteins, and the binding of heparin to antithrombin and thrombin specifically, differ significantly across neonates, children, and adults (5). More recently, plasma proteomic analysis demonstrated age-specific changes in platelet- and endothelial cell-derived proteins and regulators of coagulation and fibrinolysis, underscoring that the hemostatic profile of neonates is uniquely distinct even within the pediatric range (7).

From a clinical laboratory perspective, my work confirmed developmental hemostasis using modern coagulation analyzers, demonstrating that reference values are both age-dependent and reagent-dependent, requiring each laboratory to establish its own age-specific normative data (8).

Epidemiology and risk factors

The overall incidence of VTE in children is low (0.7 to 4.9 per 100,000 per year), rising 100- to 1,000-fold among hospitalized children. A bimodal age distribution is consistently observed: the neonatal period accounts for approximately 20% of pediatric VTE and adolescence for approximately 50% (9).

In neonates, more than 90% of VTE episodes are associated with CVCs. Neonatal VTE encompasses catheter-related VTE, renal vein thrombosis, and cerebral Sinovenous thrombosis. Additional neonatal risk factors include low gestational age, sepsis, polycythemia, and maternal conditions such as diabetes mellitus and antiphospholipid syndrome. The neonatal hemostatic system is not intrinsically prothrombotic but is extremely sensitive to acquired insults that shift the molecular hemostatic balance toward thrombosis, a vulnerability that reflects the physiological differences documented at the protein level.

In older children and adolescents, acquired risk factors such as malignancy, congenital heart disease, obesity, infection, surgery, L-asparaginase therapy, and oral contraceptive use are consistently identified.

Diagnosis: challenges in the pediatric context

Pediatric VTE diagnosis is challenging due to non-specific and age-variable presentations. Neonates may show swelling, discoloration, or organ dysfunction, while older children may report limb pain or dyspnea.

Compression ultrasonography with Doppler imaging is the first-line modality for suspected deep vein thrombosis. Echocardiography is essential for intracardiac thrombosis, while MRI or CT pulmonary angiography may be required for cerebral Sinovenous thrombosis or pulmonary embolism, with consideration of radiation exposure and sedation needs in young children. As previously mentioned, laboratory evaluation must use age-specific reference ranges, as adult-derived ranges are inappropriate.

D-dimer has limited utility in children, as age-specific cutoffs are not universally validated and D-dimer is elevated by numerous non-thrombotic conditions in hospitalized children. Thrombophilia testing should be deferred until after anticoagulation is stopped and ideally until the child is older, given developmental regulation of coagulation proteins. Clinically unsuspected (e.g., incidentally detected) VTE is an important unresolved area in pediatric practice since its natural history and need for treatment remain poorly defined, and standardized definitions and management recommendations are urgently needed (10).

Treatment of pediatric thrombosis

Until recently, pediatric VTE management relied on unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), and vitamin K antagonists (VKAs), each with significant practical limitations. The age-specific differences in heparin pharmacodynamics documented via my research explain why children, and especially neonates, require different dosing regimens to achieve therapeutic anticoagulation.

The Kids-DOTT randomized trial (2022) demonstrated that 6 weeks of anticoagulation was non-inferior to 3 months for preventing recurrent VTE in patients under 21 years with provoked thrombosis, reducing treatment burden (11).

The regulatory approval of rivaroxaban and dabigatran for pediatric VTE by the FDA in 2021 represented a paradigm shift. Rivaroxaban received approval for VTE treatment and recurrence prevention from birth to 18 years, and for thromboprophylaxis after Fontan procedure in children aged ≥2 years. Dabigatran was approved for VTE treatment in patients aged 3 months to under 18 years. Both were supported by dedicated pediatric pharmacokinetic and clinical trials (EINSTEIN-Jr (12) and DIVERSITY (13), respectively), demonstrating safety and efficacy comparable to standard-of-care. DOACs offer

oral administration, child-friendly formulations, and no routine monitoring requirement.

The 2024 American Society of Hematology (ASH) / International Society on Thrombosis and Haemostasis (ISTH) updated guidelines now formally endorse DOACs for a range of pediatric VTE indications (14). For neonates, LMWH remains the standard of care pending dedicated neonatal DOAC data.

Future directions: multi-omics in pediatric thrombosis

The most transformative future research direction is the application of multi-omics, specifically the integrated analysis of proteomics, genomics, transcriptomics, metabolomics, and epigenomics to systematically characterize the molecular underpinnings of developmental hemostasis and to identify novel biomarkers and therapeutic targets for pediatric thrombosis. My research has pioneered the proteomics dimension of this approach, establishing age-specific differences in the plasma proteome and platelet- and endothelial-derived hemostatic regulators. However, proteomics alone is insufficient: the hemostatic phenotype is shaped by gene expression, posttranslational modification, metabolic context, and epigenetic regulation, all of which change across development.

Genomic and transcriptomic profiling of children with VTE versus age-matched controls could identify susceptibility determinants beyond classical thrombophilias. RNA-sequencing across age groups would define transcriptomic correlates of the developmental proteomic transitions already documented, linking gene expression to hemostatic phenotype.

Epigenomic profiling could reveal how developmental changes in DNA methylation and histone modification regulate coagulation gene expression, providing a mechanistic link between the developmental clock and the hemostatic phenotype, and offering stable biomarkers of cumulative thrombotic risk in children with chronic conditions.

Metabolomic profiling could identify circulating biomarkers of thrombotic risk reflecting inflammatory, endothelial, and platelet metabolic states, thus providing the basis for next-generation, age-validated pediatric VTE risk scores that do not rely on adult extrapolation.

Integrative multi-omics analysis combines proteomics, metabolomics, and genomics in the same cohorts, and has the potential to enable construction of comprehensive molecular networks of hemostatic regulation across development. Such networks could identify key regulatory nodes differing between children and adults, explaining the transition from thromboprotection in neonates to rising VTE susceptibility in adolescents, and reveal why anticoagulants behave differently across age groups.

Finally, artificial intelligence (AI) applied to multi-omics datasets from large, age-stratified pediatric cohorts could power clinical decision support tools guiding thromboprophylaxis, anticoagulant selection, and treatment duration in a personalized, developmentally informed manner. Realizing this vision requires age-stratified pediatric biobanks, international data-sharing, and normative multi-omics atlases in healthy children as the reference framework for interpreting thrombotic states.

Conclusions

Pediatric thrombosis is a distinct clinical entity demanding age-specific approaches to diagnosis, risk stratification, and treatment. My research and research from others has established that age-specific differences in the hemostatic system extend far beyond functional coagulation tests to encompass plasma protein composition, fibrinogen structure, platelet biology, and heparin-binding interactions. These molecular differences explain the epidemiological patterns of pediatric VTE and clinically observed variability in anticoagulant response across the age spectrum. The approval of rivaroxaban and dabigatran, endorsed by 2024 ASH/ISTH guidelines, marks one of the most significant advances in pediatric anticoagulation in decades. Looking forward, by building on the already established proteomic foundations, via multi-omics integration and utilization of AI promises to transform our understanding of developmental hemostasis to enable truly personalized thrombosis care for children.

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MODERN TOOLS TRANSFORMING BLOOD GROUP DISCOVERY; THE INTERNATIONAL BLOOD GROUP REFERENCE LABORATORY EXPERIENCE

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Abstract

Accurate identification of red cell antigens and antibodies is essential for ensuring patient and donor safety in transfusion, maternal-fetal, and transplantation medicine. Routine serological and genetic methods resolve most specificities, however, occasionally a small number of individuals present with antibodies to novel or uncharacterised antigens that cannot be determined by standard methods alone. Historically, blood group antigen and system characterisation was a stepwise, time-consuming process requiring a wide range of methods. Consequently, it was often difficult to establish the link between an antigen, its encoding gene and carrier molecule that has become a cornerstone of both classification and elucidation of effective clinical need and response. The introduction of powerful molecular technologies, namely next generation sequencing (NGS) and proteomics, has enabled the analysis of all coding genes or proteins in a single test, and has greatly accelerated characterization of new blood groups. At the International Blood Group Reference Laboratory (IBGRL, Bristol, UK), serological investigations remain the essential starting point for the discovery of new alleles, antigens or systems, followed by targeted genetic and functional studies helping to characterize new blood groups. In the last 25 years, IBGRL has described 53 new antigens and 4 new systems, of which three systems have been identified in the last six years using NGS.

Keywords: red cell antigens, blood group systems, next generation sequencing

History and evolution of red cell antigen detection methods

The discovery of the ABO system more than a century ago provided the first insight into the importance of blood groups in transfusion medicine. Since then, the most advanced contemporary methods available have been used to identify and characterize red cell antigens and their corresponding alloantibodies. During the first 45 years of the 20th century progress was slow, constrained by the limits of available methodology. The identification of new antigens relied almost exclusively on deliberate immunization of animals, observations of direct agglutination and crossmatch compatibility, resulting in the recognition of only three new systems (MNS, P1PK and RH).

The steady rate of antigen discovery increased significantly following the development of the indirect antiglobulin test (IAT) in 1945 (1), alongside further innovations in serology, biochemistry, and later molecular biology. As transfusion therapy expanded, many alloantibodies and their respective antigens were identified as direct causes of hemolytic disease of the fetus and newborn or adverse transfusion reactions. Before the advances in molecular biology and the elucidation of DNA structure in 1953, several antigens had been organised into systems (LU, KEL, LE, FY, JK). Additional eight systems (DI, YT, XG, SC, DO, CO, LW, CH/RG) were established prior to the development of transformative molecular techniques such as Sanger sequencing (1977), Western blotting (1979), and polymerase chain reaction (PCR; 1983). New biochemical methodologies, including thin-layer chromatography, SDS-polyacrylamide gel electrophoresis, and Western blotting, enabled the classification of antigens as either carbohydrates or proteins, whilst the development of monoclonal antibodies improved antigen detection, particularly for those antigens expressed in low copy numbers. In terms of blood group genetics, the initial progress was achieved with the first chromosomal assignment of the gene *ACKR1* (FY) in 1968 (2), and later with the cloning of *GYPA* (MNS) in 1986 (3), which opened the way for the exploration for blood group genes. By the end of 20th century, most major blood group antigens and systems had been defined.

The new century has seen a combination of multiple sequencing technologies

leading to the publishing of the Human Genome Project in 2004; a landmark reference sequence that allowed more reliable assessment of blood group-related variants. This reference sequence led to an exponential rate of discovery of new antigens and systems, especially when combined with the new transformative technologies of next generation sequencing (NGS), genome-wide association studies (GWAS), various -omics methods (proteomics, genomics, transcriptomics), and

bioinformatics. In the last 25 years, nearly half (48%) of all known blood group systems have been identified, which is comparable to the number of systems identified in the 100 years previous to this. The 18 newest established systems were all characterised using either NGS, GWAS, proteomics, in silico analysis or a combined approach (4).

In 1980, the International Society of Blood Transfusion (ISBT) established the Working Party (WP) for Red Cell Immunogenetics and Blood Group Terminology (RCI&BGT) to standardise nomenclature and ensure consistency in this rapidly expanding field; it continues to oversee allele, antigen and system designation today (4).

ISBT criteria for establishment of new blood group antigens and systems

The core criteria for the assignment of a new antigen to an existing system are the detection of a corresponding alloantibody and evidence that the antigen is an inherited character. The minimal proof typically involves characterization of the variation in the gene controlling the system and demonstration that the antigen is located on a protein or glycoprotein that carries other antigens of the respective system.

The core criteria for the establishing a new system are the same as for a new antigen, i.e. the antigen must be defined by an alloantibody, and it must be an inherited character, however additional, more stringent evidence is required. The gene encoding the antigen(s) of the proposed system must be identified, sequenced, and mapped to a specific chromosomal location. It must also be distinct from, and not a closely linked homologue of, genes encoding antigens of any existing blood group system. Furthermore, expression on red cell or erythroid progenitors, as well as comprehensive expression studies, must be demonstrated.

At present, ISBT recognises 398 antigens, of which 371 antigens are assigned to 48 systems. The remaining 27 lack fully elucidated genetic bases and are therefore classified as “orphan” antigens within the collections (200), low (700) or high (901) prevalence antigen series. The ISBT RCI&BGT WP meets annually to evaluate evidence for new antigens and/or systems ratification, including the molecular characterization of the known orphan antigens or identification of entirely novel *de novo* antigens (4).

Blood group discovery in international blood group reference laboratory

The International Blood Group Reference Laboratory (IBGRL), established by the UK Ministry of Health in 1946, originally initiated a centralised production of blood-grouping reagents and provided a red cell reference service for the newly formed National Blood Transfusion Service. It has since evolved into an international tertiary reference laboratory specializing in complex red cell antigen and antibody investigations and blood group genetics. IBGRL also hosts the NHS Blood and Transplant Rare Donor Screening Programme, manages the National Frozen Blood Bank, and maintains the International Rare Donor Panel. Additional functions include training, education, and importantly, research focused on blood group discovery.

Annually, the laboratory receives approximately 800 complex cases from the UK and abroad, involving problems of unresolved antibody specificity or antigens of unresolved genetic bases. All investigations start with serological analyses, and more than half of the cases are resolved at this stage. When serology is inconclusive, cases progress to genetic studies guided by the serological findings and may involve a variety of genotyping and DNA sequencing methods. The choice of method depends on the level of detail required. As the simplest option, genotyping is used to investigate and/or confirm known blood group polymorphisms (e.g., $Fy^{a/b}$, K/k). If strong serological clues suggest that a phenotype may be associated with a particular system, this typically leads to the use of Sanger sequencing of the relevant gene(s). However, in the absence of serological clues, wider NGS strategies are employed. One of the major advantages of a sequencing-based strategy is the ability to identify new and previously unreported genetic variants, which cannot be detected by genotyping alone.

To support routine testing, IBGRL has developed an NGS-based in-house custom designed blood group gene panel that allows simultaneous sequencing of all known blood group-associated genes for multiple samples in a single sequencing run, providing a complete blood group genetic profile in timely and cost-effective manner. The panel is updated annually to include newly recognised system genes by ISBT RCI&BGT WP. Following genetic work-up, most cases are resolved as known blood group variants, while a minority reveal novel alleles, antigens, or occasionally new systems. Amongst more than 300 complex cases tested to date using the panel, 53 new variants have been identified in known blood group genes: 40 encoding new alleles and 13 encoding new antigens in established systems. However, even with the good resolution rate, approximately 6% of cases remain unresolved and those with suspected novel blood group phenotypes are progressed to whole exome sequencing to search for potential candidate genes that could explain those phenotypes. Once the rare variants in potential candidate genes are identified and evaluated, the most promising candidates are selected for more in-depth studies.

Proof-of-function methods vary depending on the complexity of the variants, but most investigations involve gene editing and in vitro expression studies to establish a link between the genetic variant and the observed phenotype. At IBGRL, this typically includes CRISPR-based knockout of the endogenous gene of interest followed by rescue with wild-type and variant constructs.

For a new blood group system, proof work must unequivocally demonstrate expression of the antigen carrier on red cells or erythroid precursor cells and confirm that the genetic variant encodes the observed phenotype. Additional characterization, including population frequency data, protein modelling, expression during erythropoiesis and any available physiological and clinical evidence is compiled in support of the case. Unlike new systems, new antigens usually require fewer follow-up studies because both the system and its encoding gene are already known. The extent of expression and functional investigation depends on the antigens' prevalence and current understanding of their carrier molecules. For both new systems and new antigens, the evidence is submitted to the ISBT RCI & BGT WP for ratification. Once approved, they are added to the database of recognised blood group variants and can subsequently be integrated into future genetic testing strategies and patient care.

The Identification of the genetic and protein background of blood groups is today regarded as routine, and there is growing emphasis on expression studies to verify candidate genes and/or proteins identified through powerful methods of NGS and proteomics.

Using this process, four genes have recently been identified and confirmed as responsible for the expression of new blood group systems: MAM (5), ER (6), MAL (7), and JAMA (tbc). Several additional candidate genes are currently under investigation to establish definitive links between genetic variants and observed phenotypes.

Examples of new antigen and system characterization in IBGRL

In our latest blood group system study, we investigated AnWj, a high prevalence antigen first described in 1972 with no known molecular basis but linked with severe heamolytic transfusion reactions. AnWj-related antibodies are rare and are usually associated with the transient suppression of AnWj expression, although a small number of individuals have a persistent, inherited AnWj-negative phenotype. Using whole exome (NGS) and Sanger sequencing, we demonstrated that the inherited AnWj-negative phenotype was defined by a large homozygous deletion of exons 3 and 4 of the *MAL* gene, encoding myelin and lymphocyte protein (Mal). We confirmed Mal was the carrier molecule for the AnWj antigen through immunoblotting experiments, CRISPR/Cas9-mediated gene knockout and expression studies, thus providing evidence for the ratification of the new system by the ISBT RCI&BGT WP in 2024 (7).

Since 2024, we have identified four new, extremely rare antigens, now added to their respective systems by the ISBT RCI&BGT WP: BROS to CTL2 (CTL2_05), LULO to Lutheran (LU31), CRIB to Cromer (CROM21) and SCIBB to Scianna (SC11). BROS (8), LULO (9) and CRIB (10) are high prevalence antigens detected in patients with antigen-negative phenotypes that were shown to be caused by homozygosity for new missense variants in their respective genes, whilst SCIBB is a low prevalence antigen, shown to be defined by a new heterozygous variant in *ERMAP*, the gene encoding antigens of the Scianna system (11). All four antigens underwent extensive serological and genetic analyses, supported by protein modelling. Expression studies in HEK and MOLT4 cell lines confirmed the causative effect of the variants and the expression of BROS, LULO and SCIBB. These findings again demonstrate the value of integrating serology, NGS, protein modelling and cell-based expression systems for timely and accurate characterisation of new blood group antigens.

The future

Sophisticated molecular tools, mainly NGS and proteomics, have been responsible for a dramatic increase in the discovery of new blood group systems, including EMM (ISBT42) (12), ABCC1 (ISBT43) (13) discovered by whole genome sequencing and CTL2 (ISBT039) (14), PEL (ISBT40) (15), MAM (ISBT41) (5), ER (ISBT44) (6), ATP11C (ISBT46), MAL (ISBT47) (7) and PIGZ (ISBT48) (17) discovered by whole exome sequencing. In the future, although only 27 orphan blood group antigens now remain unresolved, there may be many rare *de novo* antigens discovered, as seen in the study of the newest ratified antigen GWADA (PIGZ system) (17), found in the only one individual in the world who is lacking this high prevalence antigen. This momentum in the blood group characterisation will not end with the currently recognised 48 systems. Technologies, such as third generation sequencing and integration of artificial intelligence, machine learning and advanced bioinformatics will ensure the continued development of our understanding of blood groups within biomedicine and personalised patient care.

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CURRENT MANAGEMENT OF THROMBOTIC THROMBOCYTOPENIC PURPURA

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Thrombotic thrombocytopenic purpura (TTP) is a rare but potentially fatal thrombotic microangiopathy characterized by severe ADAMTS13 deficiency occurring either as immune-mediated TTP (iTTP) or congenital TTP (cTTP). ADAMSTS13 deficiency provokes the accumulation of ultra-large von Willebrand factor multimers (ULvWFM) and the development of platelet-rich microvascular thrombosis, leading to the characteristic signs and symptoms of the disease: thrombocytopenia, schistocytes and multiple organ dysfunctions. In suspected acute iTTP, treatment should be initiated promptly, before confirmatory ADAMTS13 testing is available, given the high risk of early morbidity and mortality.

A better understanding of the pathophysiology of iTTP, together with the availability of targeted therapies, allows us to apply a strategy that aims to act at three levels: 1. Blocking the binding of platelets to the ULvWFM. 2. Removal of circulating antibodies against ADAMTS-13 and 3. Inhibiting the production of ADAMTS-13 inhibitor antibodies. In practice, this translates into the combination of early administration of caplacizumab to block the adhesion of platelets to ULvWFM and thus preventing tissular ischemia and hasten platelet count normalization. The removal of circulating antibodies can be effectively achieved through daily or alternate-day plasma exchange, using fresh frozen plasma and/or albumin as the replacement solution. The addition of intravenous immunoglobulin at replacement dose, adds an immunoprotective and immunomodulatory effect to plasma exchange. Nowadays the inhibition of the production of new antibodies against ADAMTS-13 is realized by the combination of administration of oral corticosteroids, and once the severe deficit and the inhibitory antibodies against ADAMTS-13 are confirmed, by the administration of rituximab, for targeting B-cell–mediated autoantibody production and for reducing the risk of exacerbation and relapse.

Supportive management requires close assessment of neurological, cardiac, renal, and hemorrhagic complications, while platelet transfusion is generally reserved for life-threatening bleeding. During remission, serial ADAMTS13 monitoring is clinically relevant because declining activity may precede relapse and support pre-emptive immunosuppression. In cTTP, long-term ADAMTS13 replacement is the principal treatment objective, with recombinant ADAMTS13 preferred where available and plasma infusion remaining an alternative when access is limited.

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TRENDS AND CHALLENGES IN BLOOD AND PLASMA COLLECTION AND USE IN EUROPE

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Abstract

European transfusion medicine systems are currently facing major demographic, organisational and clinical challenges affecting the collection and use of blood components, including plasma for fractionation. This paper analyses recent trends in the collection, supply, and use of blood and blood components across Council of Europe member states between 2020 and 2023, examines the economic and clinical value of plasma-derived therapies, and reviews structural vulnerabilities in the European supply chain. Data reveal statistically significant increases in whole blood donations, first-time donors, platelet preparation and transfusion, and plasma collected for fractionation, while the number of plasma units transfused declined. Red blood cell demand remains substantial but is increasingly influenced by Patient Blood Management strategies, while platelet utilisation continues to grow because of advanced oncological and haematological treatments. Despite these positive developments, important heterogeneity persists among European countries regarding donor recruitment, collection infrastructure, plasma self-sufficiency, and organisational models. Plasma has emerged as a strategic healthcare resource, yet Europe remains dependent on imports, primarily from the United States, for approximately 40% of plasma required for fractionation. Major challenges include ageing donor populations, recruitment and retention of younger donors, logistical complexity, economic pressures, ethical debates concerning donor compensation, and the need for stronger European strategic autonomy.

Keywords: Blood transfusion; Plasma-derived medicinal products; European strategic autonomy.

Introduction

Blood and plasma are unique biological resources whose collection depends entirely on voluntary human donation. They underpin two distinct but interconnected therapeutic domains: transfusion medicine (red cells, platelets, plasma for direct clinical use) and the industrial fractionation of plasma into life-saving medicinal products such as immunoglobulins (IG), albumin, and coagulation factors.

Over recent decades, European transfusion medicine has undergone profound changes driven by demographic ageing, evolving clinical practices, technological innovation, increasing therapeutic complexity, and growing demand for plasma-derived therapies (1–3). At the same time, blood establishments have faced major organisational and operational challenges associated with donor recruitment, economic sustainability, inventory management, and regulatory harmonisation; this latter became particularly prominent after the substantial modification of the Regulatory Framework and Policy Responses following the approval of the Regulation (EU) 2024/1938 (SoHO Regulation) (4). Key provisions of the Regulation, intended to replace all previous Blood Directives, include: mandatory national monitoring and emergency planning for critical SoHO supply; reaffirmation of voluntary unpaid donation; establishment of the SoHO Coordination Board for EU-level governance; and enhanced vigilance and traceability via the SoHO Platform.

The European Committee on Blood Transfusion (CD-P-TS) of the European Directorate for the Quality of Medicines & HealthCare (EDQM) systematically monitors activities related to blood collection, preparation and use across Council of Europe member states. Its 2020–2023 report (5), complemented by the EU-funded SUPPLY project (6) and recent economic analyses (1, 7), provides a comprehensive picture of an evolving landscape characterised by rising demand, supply vulnerabilities, and pressing policy challenges.

This paper synthesises these recent findings to identify the dominant trends in blood and plasma collection and use, the structural risks confronting Europe, and the policy directions likely to ensure sustainable supply.

Methods and data sources

The analysis draws primarily on the EDQM CD-P-TS 2020–2023 report covering 38 member states, with response rates averaging 95% across the four reporting years . Complementary evidence is drawn from the SUPPLY project deliverables and reports on scenario planning, legal frameworks and PDMP management (6), and from economic assessments of plasma-derived therapies in Europe (1, 7).

Donor Population

Donors who donated at least once per year showed a statistically significant positive trend of +1.1% annually. First-time donors increased by +3.4% per year, with consistent growth in Greece, Hungary, Lithuania, Moldova, Serbia, and Spain. The median proportion of first-time donors was 17%, ranging from 8% in Malta to 55–70% in Albania and North Macedonia. Recent analyses confirm that demographic ageing across Europe threatens long-term donor base sustainability, with estimates suggesting a 10–15% reduction in eligible donors by 2035 in several Western European countries (2).

Whole Blood and Component Collection (RBC and Platelet)

Whole blood collection increased by 2.1% per year, Germany remaining the largest collector (3.7 million units in 2023). Platelet apheresis grew by 2.1% per year, while granulocyte collection declined by 11.4% annually—the strongest negative trend, reflecting limited clinical use.

Blood Component Use (RBC and Platelet)

Red blood cells remain the most frequently transfused blood component in Europe. EDQM analyses demonstrated positive trends both in the preparation of red cell units and in actual transfusion activity. Red cell units prepared and transfused both increased significantly (+1.9% and +1.4% per year). However, the substantial stability in RBC demand is the net result of countries increasing RBC transfusion while in many others figures reflect a decrease in use, related to Patient Blood Management PBM strategy adoption. PBM programmes aim to optimise patient outcomes while reducing unnecessary transfusions through restrictive transfusion thresholds, perioperative anaemia management, minimisation of blood loss, and evidence-based clinical protocols; they have become increasingly important throughout Europe.

Platelet units prepared and transfused grew by +2.6% per year. Platelets represent one of the fastest-growing blood components in modern transfusion medicine (8). EDQM analyses demonstrated statistically significant positive trends in platelet collection, preparation, and transfusion activity between 2020 and 2023. Platelet apheresis collection increased by approximately 2.1% annually, while platelet transfusions increased by approximately 2.6% per year. This increase reflects the growing complexity of modern healthcare, particularly in oncology, haematology, stem cell transplantation, and intensive chemotherapy. Improved survival of patients with haematological malignancies has substantially increased long-term platelet demand. Advanced oncological therapies, including CAR-T cell therapy and aggressive immunosuppressive treatments, also contribute to rising platelet utilisation. Pathogen reduction technologies are increasingly implemented for platelet safety enhancement. However, these technologies substantially increase production costs and may create financial challenges for smaller blood establishments.

Plasma Collection and Use

Plasma currently occupies a central strategic role in European healthcare systems.

Fresh frozen plasma remains essential for transfusion medicine, particularly in trauma care, massive haemorrhage, liver disease, and coagulation disorders. However, Fresh Frozen Plasma (FFP) units transfused declined by 2.3% per year. This reduction likely reflects improved evidence-based plasma utilisation, implementation of PBM strategies, and increased use of targeted coagulation therapies (9).

On the other hand, plasma is increasingly important as the raw material for the production of plasma-derived medicinal products, including immunoglobulins, clotting factors, albumin, and alpha-1 antitrypsin. Approximately 1.12 million Europeans live with the twelve most common rare diseases treatable with PDMPs, including primary immunodeficiency (PID), haemophilia A and B, von Willebrand disease, hereditary angioedema, alpha-1 antitrypsin deficiency, and chronic inflammatory demyelinating polyneuropathy (CIDP) (1). Recognition of secondary immunodeficiency (SID) in haematological malignancies and following CAR-T therapy is rapidly expanding immunoglobulin demand. The Europe immunoglobulin market is estimated to develop with a CAGR of 6.9% over the forecast period of 2022 to 2030 (10).

Plasma collected for fractionation increased significantly (+1.3% per year). Germany dominated absolute volumes (3.35 million litres in 2023), with growth in Czechia, Denmark, Spain, Italy and in the United Kingdom where plasma collection has started again after the removal of UK resident ban for vCJD. Twelve member states reported no plasma collection for fractionation, highlighting persistent disparities. According to the conclusions of a recent international symposium (11), this fragmentation undermines the EU capacity to achieve strategic autonomy and necessitates coordinated cross-border collection strategies.

Europe's dependence on imported plasma

Despite increased collection activity, Europe remains heavily dependent on imported plasma, particularly from the United States (1, 12). Current estimates indicate that Europe still imports approximately 40% of the plasma required for fractionation into PDMPs. The growing demand for immunoglobulins represents a major driver of plasma demand. This dependence has generated increasing political and scientific concern regarding healthcare resilience, strategic autonomy, and long-term security of supply.

Plasma collection models and ethical debates

European countries apply heterogeneous organisational models for plasma collection (13). Some countries maintain exclusively voluntary non-remunerated donation systems, whereas others permit compensated plasma donation and private plasma collection centres. Germany, Austria, Hungary, and the Czech Republic currently report among the highest plasma collection volumes in Europe because of mixed public-private systems and compensated plasma donation policies.

This heterogeneity has generated continuing ethical debate regarding donor compensation, voluntary donation principles, and healthcare equity. The principle of voluntary unpaid donation remains central to European blood policy, yet increasing plasma demand has stimulated discussions regarding ethically acceptable compensation mechanisms (14). Particularly relevant in this context is the SUPPLY project, a project co-funded by the European Union's EU4Health Programme that aims to increase and strengthen the resilience of plasma collection in the EU to enable a stable and adequate supply of Plasma-derived medicinal products (PDMPs) (6).

As main conclusions of the project, documents released recommend a systemic approach combining legal frameworks recognising plasma as a strategic resource, cooperation between public non-profit and private for-profit sectors, harmonised cross-border collaboration, and prioritised use of products from domestic plasma (15). Importantly, the existing voluntary non-remunerated donor base, which currently supplies 100% of European needs for blood components other than plasma for fractionation, must be protected (6).

Safety, quality, and regulatory evolution

European transfusion medicine systems maintain some of the highest safety standards globally. Donor screening, infectious disease testing, haemovigilance systems, quality assurance programmes, and traceability procedures are highly developed throughout Europe.

The European SoHO (Substances of Human Origin) Regulation (4) represents an important regulatory evolution intended to harmonise standards for blood, plasma, tissues, and cells across the European Union. The regulation aims to strengthen donor protection, improve cross-border cooperation, enhance traceability systems, and ensure greater preparedness for future healthcare emergencies.

Conclusions

European blood and plasma collection systems are currently undergoing major structural transformation.

Red blood cell utilisation is increasingly shaped by Patient Blood Management programmes and evidence-based transfusion practices. Platelet demand continues to grow because of increasingly advanced oncological and haematological treatments. Plasma has emerged as a strategic healthcare resource because of expanding demand for plasma-derived medicinal products. A new regulatory framework, the European SoHO (Substances of Human Origin) Regulation, is expected to promote safety, quality, availability and accessibility for blood products, while protecting the rights of both donors and recipients.

However, significant challenges remain. Demographic ageing, increasing platelet and plasma demand, economic pressures, donor retention difficulties, and growing organisational complexity threaten long-term sustainability. Ensuring safe, sustainable, and equitable access to blood and plasma products throughout Europe will require coordinated investment, technological innovation, harmonised regulation, workforce development, and long-term political commitment.

The future resilience of European transfusion medicine will depend not only on maintaining donor participation but also on strengthening strategic autonomy, particularly in plasma collection and fractionation capacity.

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SERBIAN BLOOD TRANSFUSION SERVICE - ON THE PATH TO THE EUROPEAN UNION

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Abstract

This paper analyzes the organization and development of the blood transfusion service in Serbia in the context of alignment with European regulations and World Health Organization (WHO) recommendations, with special emphasis on the safety, availability, and sustainability of blood supply. The goal of the reorganization is to improve and standardize the quality of work. Attention is given demographic changes, population migration, different generational communication styles, and maintaining the continuity of voluntary, non-remunerated blood donation.

Organizational models in European countries are analyzed, highlighting the role of centralization and system rationalization. Blood safety is ensured through strict donor screening, mandatory testing for transmissible infections, and the application of quality standards. The importance of national policy and integrated blood supply systems is also considered, as well as the role of the WHO in the global improvement of this field.

The preparation of blood and blood components includes the activity of promotion, planning, collection and testing, processing, storage and distribution of blood/ blood components is carried out in Blood establishments (seven). Serbian transfusion service functions as a coordination service

Previous results indicate that Serbia has made significant progress in implementing WHO and EU SoHO standards, but further alignment and strengthening of the system is required by 2027.

Key words: reorganization, safe blood, EU and WHO recommendations

Sažetak

Rad analizira organizaciju i razvoj službe transfuzije krvi u Srbiji u kontekstu usaglašavanja sa evropskim regulativama i preporukama SZO, sa posebnim osvrtom na bezbednost, dostupnost i održivost snabdevanja krvlju. Osnovni cilj reorganizacije je unapređenje i ujednačavanje kvaliteta rada, kao i efikasnije upravljanje rezervama krvi i krvnih komponenti. Posebno se ističu izazovi kao što su demografske promene, migracije stanovništva, različiti komunikacioni stilovi generacija i održavanje kontinuiteta dobrovoljnog, neplaćenog davanja krvi.

Analizirani su modeli organizacije u evropskim zemljama i naglašena je uloga centralizacije i racionalizacije sistema. Bezbednost krvi se obezbeđuje strogim skriningom davalaca, obaveznim testiranjem na transmisivne infekcije i primenom standarda kvaliteta. Takođe se razmatra značaj nacionalne politike i integrisanih sistema snabdevanja krvlju, kao i uloga SZO u globalnom unapređenju ove oblasti.

Reorganizacijom Služe transfuzjije ostvarenaje kroz ukrupnjavane. Ppriprema krvi i komponenata krvi obuhvata delatnost promocije, planiranja, prikupljanja i testiranja, obrade, čuvanja i distribucije krvi i komponenata krvi i obavlja se u ovlašćenim transzijskim ustanovama (OTU) kojih ima sedam. Transfuziološka služba Sbrije nije jedinstvena, ali funfcioniše kao kooredinisna služba Dosadašnji rezultati ukazuju da je Srbija ostvarila značajan napredak u primeni SZO i EU SoHO standarda, ali da je potrebno dalje usaglašavanje i jačanje sistema do 2027. godine.

Ključne reči: reorganizacija, bezbedna krv, preporuke EU i SZO

Serbia, as a country that has committed itself to the European path, shares European values and geographically belongs to Europe. Within the operations of the Blood Transfusion Service, it respects the postulates of European Union (EU) regulations related to substances of human origin (SoHO) (1). The main task of the transfusion service is to ensure sufficient quantities of safe blood. In fulfilling this task, sustainable growth of regular, voluntary unpaid donation is encouraged, along with raising awareness of the impact of blood donation and saving lives, emphasizing the vital contribution of blood donors, and promoting the values of solidarity and humanity (2).

The first problem is ensuring sufficient quantities of blood/blood components through an adequate number of voluntary blood donation drives and sufficient participation of voluntary blood donors (VBD) (3). The outflow of working-age people-potential blood donors in their best years-represents a significant problem in several countries, including Serbia (4). There is also the problem of social alienation in places with more than 600,000 inhabitants, making it more difficult to convey messages related to voluntary blood donation in such environments. New generations of young people, Millennials and Generation Z, have developed different ways of communication, which presents a challenge for adapting the messages of the Transfusion Service to their communication styles (5).

Special emphasis is placed on blood safety. Advances in science, testing, and blood safety systems have made transfusion safer than ever, but safe blood still depends on people willing to donate regularly and voluntarily. Many countries still face shortages and unequal access to safe blood/blood components (1, 2).

The first step is the reorganization of the service through the consolidation of smaller transfusion institutions, and this should be a one-way process without reversal. There should be no exceptions to the rules or changes in regulations during the implementation of the reorganization (6). Almost all European countries have undergone a process of reorganization and consolidation (except Italy) Switzerland has opted for a gradual transition from 11 to 4 blood transfusion centers. Croatia, which is geographically closest and comes from the same transfusion school and is similar to Serbia in some aspects, represents a combined model that could be applied in Western Balkan countries (7 centers: 5 for collection, processing, and testing; 2 for collection and processing, with samples sent to another center/Zagreb, where testing is performed). Spain is an example of a country that has entered reorganization but still maintains a relatively large number of centers—17 transfusion institutions.

The main goal and reason for the reorganization of the service is to improve and standardize the quality of work of transfusion services, and to develop good management of reserves with a clear definition of minimum and maximum required quantities (1, 2). One of the major problems that arises during this process is the mistrust of smaller centers that are being integrated. Together with an already reduced number of individuals eligible to be VBD, and different communication methods across various environments and generations, this can lead to a temporary decrease in the number of donors (5).

Blood donation requires the creation of a positive environment in which active citizens consider it a natural right to donate blood and thereby contribute to the well-being of their fellow citizens. It is necessary to develop a culture of solidarity and create a sense that it is a citizen's right to donate blood on the day they turn 18- legal adulthood is reached (7).

The problem of migration of working-age individuals can be addressed by improving economic conditions, but also by developing a sense of belonging to the community and a desire to help that same community in every way, both economically and through acts of solidarity such as blood donation.

The main difference is that Millennials generally prefer more detailed, structured, and contextual communication, while Generation Z tends to communicate in a shorter, faster, and more visual way, using memes, emojis, and short video formats (4). We are witnessing artificial intelligence entering all areas of society, so we can expect it to also find its place in promoting blood donation, but in doing so, compliance with Directive (EU) 2022/2555 must be respected.

In most European countries, healthcare systems take care of blood donors. The need to balance costs exists even in the most developed countries. However, each country makes efforts to reduce the significant costs of safe transfusion practices, based on the rational use of blood/blood components, thereby optimizing blood consumption and the required number of donations.

A good example of reorganization and rationalization is Finland. The system operates through 10 centers that collect blood, while only one processes and tests it. From this single institution, distribution is carried out via regular postal services, bus transport, air transport for the most remote northern areas, and private courier services. The further goal of rationalization foresees reducing the annual number of mobile teams and focusing on fixed donation locations. Finland is also a good example of a balanced sense of responsibility toward supporting the local community. The more developed south of the country could cover the needs for blood/blood components in the north, but donation drives in the north are still maintained due to residents' desire to contribute to the healthcare system.

Scotland which has long been a leader in promoting voluntary blood donation and a pioneer in certain approaches to communicating with potential donors, suffered significant damage to voluntary donation efforts due to Cambridge Analytica and the misuse of personal data on Facebook for political purposes. This led to a shift toward direct communication with donors via SMS and email, as well as the use of traditional media channels – newspapers, television, and radio – suggesting a stronger reliance on public relations.

It is necessary to properly balance the use of traditional and modern communication tools and ensure donor protection both in terms of physical health and electronic data security.

Since 1975, the WHO has consistently emphasized the global imperative of blood safety and availability through the adoption of multiple resolutions. These actions have elevated blood safety as a priority within global and national health agendas.

Today, the WHO Blood Programme operates within the Department of Health Products Policy and Standards . Together

with other programs in the department, it contributes to achieving WHO strategic objectives: strengthening national health systems and ensuring universal access to health services, health products, and technologies. The cornerstone of these efforts is the Global Database on Blood Safety (GDBS), which collects and consolidates essential data from countries worldwide (8).

These data cover indicators across the entire transfusion chain providing a robust evidence base for policy dialogue and decision-making. GDBS global status reports inform WHO global strategies on blood safety and support initiatives such as the WHO Action Framework for improving universal access to safe, effective, and quality blood products 2026–2030. Data analysis has shown that in 70% of countries, funding for transfusion services is provided either from government budgets or reimbursement systems, it is essential that all member states establish a system that ensures sustainable, adequate, and consistent funding for blood programs.

This system should be aligned with the broader national framework for healthcare financing. It is important that such a system does not create financial barriers for patients who require blood transfusion. It can be said that current blood donations come from all types of donors: voluntary non-remunerated, family or replacement, and paid donors. In GDBS surveys, only 10 countries reported that they were unable to test 100% of collected blood for one or more infections.

The prevalence of infection among blood donors, or the proportion of blood donations with positive results, is directly related to the safety of the blood supply, as it affects the residual risk in distributed blood components for transfusion, as well as the risk arising from errors in quarantine and blood release. The prevalence of infection in blood donations depends on the prevalence of infection in the population from which donors are selected and on the effectiveness of donor recruitment and selection processes (8).

The quality and safety of blood donations are ensured through rigorous donor screening, voluntary donation systems, and mandatory testing for infections such as HIV and hepatitis. High-quality, safe blood requires donors to be healthy, well hydrated, and to avoid high-fat meals before donation. The application of strict standard infection testing is essential.

Donors undergo medical examinations to ensure their safety and the safety of recipients, and each blood donation is screened for infections. The safest blood comes from voluntary, non-remunerated, and regular donors. All equipment used for collection is sterile, new, and single-use (8).

The WHO recommends that all activities related to the collection, testing, processing, storage, and distribution of blood be coordinated at the national level through efficient organization and integrated blood supply networks. The national blood supply system should be regulated by national blood policy and a legislative framework in order to promote uniform application of standards and consistency in blood and blood product quality and safety (8).

It is extremely important to encourage governments and partners to strengthen and invest in national blood programs in order to achieve universal access to safe blood transfusion.

Data on the gender profile of blood donors show that globally, 33% of blood donations are given by women, although this varies significantly. The age profile of donors shows that proportionally more young people donate blood in low- and middle-income countries than in high-income countries. Demographic information on blood donors is important for designing and monitoring recruitment strategies (4).

An adequate and reliable supply of safe blood can be ensured through a stable base of regular, voluntary, non-remunerated blood donors. These donors are also the safest group, as the prevalence of blood-borne infections is lowest among them. World Health Assembly Resolution WHA63.12 calls on all Member States to develop national blood systems based on voluntary non-remunerated donations and to work toward self-sufficiency.

WHO recommends that all blood donations be tested for infections prior to use. Screening for HIV, hepatitis B, hepatitis C, and syphilis should be mandatory. Blood screening should be carried out in accordance with quality system requirements.

Blood collected in anticoagulant solution can be stored and transfused to a patient in its unmodified state. More efficient use is achieved by processing it into red blood cell concentrates, platelet concentrates, plasma, and cryoprecipitate, thereby meeting the needs of more than one patient (8).

The reorganization of the transfusion service in Serbia began with the adoption of the new Law on Transfusion Medicine. The preparation of blood/blood components includes promotion, planning, collection and testing, processing, storage, and distribution of blood and blood components, and is carried out in authorized transfusion institutions Blood establishments (BE), of which there are seven. The transfusion service in Serbia is not unified but functions as a coordinated system. The achieved level of blood donation in Serbia is 3.5%, carried out through voluntary, unpaid, and anonymous donation, respecting the principle of self-sufficiency.

The promotion of voluntary blood donation is carried out through regular campaigns, periodic drives, corporate social responsibility activities, marking of significant dates, involvement of public figures, and inclusion of different social groups.

Determining blood type is a basic prerequisite for the safe use of blood and blood components. Every donated blood unit is tested, and the ABO, Rh, and Kell blood group systems are determined, as well as the presence of irregular red cell antibodies.

In parallel, serological testing is performed in BE and NAT testing (HBV, HCV, HIV) at the Institute for Blood Transfusion of Serbia. We are located in an area where occasional outbreaks of West Nile Virus (WNV) may occur, so additional viral testing should also be considered. The rate of donations positive for markers of transmissible diseases (HIV – 0.004, HBV – 0.02, HCV – 0.009) corresponds to countries with upper-middle income levels. Processing includes the preparation of components (packed red blood cells, platelet concentrates, cryoprecipitate, and fresh frozen plasma). For transplant patients, leuko reduced components are provided.

Serbia has made significant progress in implementing WHO and EU SoHO recommendations, but further alignment with regulations planned for August 2027 remains to be completed.

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BLOOD GUIDE AND OTHER BLOOD TRANSFUSION RELATED ACTIVITIES OF EUROPEAN DIRECTORATE FOR QUALITY OF MEDICINES AND HEALTHCARE (EDQM)

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Abstract

The European Directorate for the Quality of Medicines and HealthCare (EDQM) is a Directorate of the Council of Europe, the continent's leading human rights organisation, in charge of ensuring the basic human right of access to good quality medicines and healthcare in Europe. The EDQM protects public health by: enabling the development, supporting the implementation and monitoring the application of quality standards for safe medicines and their safe use that are recognised as a scientific benchmark and applied worldwide. The EDQM perform a number of activities in the area of blood transfusion guided by the principles of promoting voluntary, non-remunerated blood donation, mutual assistance, optimal use of blood and blood components, and protection of both donor and recipient. The ultimate aim is to ensure the quality, safety and efficacy of blood and blood components and their optimal use, to increase their availability and avoid wastage in maintaining a continuity in their supply.

Keywords: EDQM, blood guide, blood transfusion

Background

The European Directorate for the Quality of Medicines and HealthCare (EDQM) is a Directorate of the Council of Europe, the continent's leading human rights organisation, in charge of ensuring the basic human right of access to good quality medicines and healthcare in Europe (1). The EDQM protects public health by: enabling the development, supporting the implementation and monitoring the application of quality standards for safe medicines and their safe use that are recognised as a scientific benchmark and applied worldwide (2) . The work of the Council of Europe in the area of blood transfusion began in the 1950s and is carried out under the aegis of the European Committee on Blood Transfusion (CD-P-TS). Since 2007, the European Directorate for the Quality of Medicines & HealthCare (EDQM), working under the European Pharmacopoeia Convention Partial Agreement, provides the Scientific Secretariat for these activities. The CD-P-TS actively promotes voluntary non-remunerated blood donation, mutual assistance, optimal use of blood and blood components and the protection of the donor and recipient. It develops technical standards aimed at ensuring the quality, safety and efficacy of blood and blood components and provides guiding principles that underpin safe blood donation. Its activities include the collection of international data and monitoring of practices in Europe, capacity building activities including the transfer of knowledge and expertise between organisations and experts through training and networking and the elaboration of reports, surveys and recommendations.

Work Programmes of EDQM

Blood Guide

The Guide to the preparation, use and quality assurance of blood components (the Blood Guide) is a compendium of widely accepted, harmonised, European standards that provide safety, efficacy and quality requirements for the preparation, use and quality control of blood components in Europe and beyond. Updated regularly, as a technical appendix to Council of Europe Recommendation No. R(95)15 (3) the Blood Guide collates the most current scientific information available to provide a comprehensive overview of the most recent advances and technical standards in the blood sector. The Blood Guide provides guiding principles to be considered for the donation of blood and blood components and includes the Good Practice Guidelines (GPG) which provide standards for the implementation of quality systems in blood establishments and, where applicable, hospital blood banks. The Blood Guide is elaborated by a dedicated working group (the GTS) composed of internationally recognised experts. In accordance with European Commission Directive (EU) 2016/1214, the GPG should be taken into account by EU member states in the implementation of quality systems in blood establishments. The Blood Guide is intended for all professionals working in the donation, collection, testing, processing, storage, distribution and transfusion of blood and blood components, for blood establishments, hospital blood banks and healthcare and regulatory professionals in the blood sector.

What's new in the 22nd Edition?

The latest edition of the Blood Guide includes a complete review of all chapters, an in-depth revision of the Haemovigilance chapter and the addition of two new chapters, Blood components for topical use or injection and Blood supply contingency and emergency planning (4). Other significant changes relate to donor selection criteria (Creutzfeldt–Jakob disease, malaria, blood pressure and pulse, plasmapheresis, iron stores, donor age and insulin). All changes are documented in a change log to facilitate uptake of the new edition and are supported by background documents detailing the scientific rationale behind them.

The 22nd edition of the Blood Guide refers to Directives 2002/98/EC and 2004/23/EC, which remain in force until 7 August 2027, in accordance with the transitional provisions of Regulation (EU) 2024/1938 of the European Parliament and the Council of 13 June 2024, concerning quality and safety standards for substances of human origin (EU SoHO Regulation).

EDQM SoHO Guides are recognised as a formal point of reference within the new EU SoHO Regulation.

Data collection and monitoring of practices

The CD-P-TS publishes annual activity reports on the donation, collection, testing, use and quality aspects of blood and blood components. Each report provides comprehensive activity data from the CD-P-TS member states and highlights new or changed practices, addressing trends in the blood sector in Europe. The collection, supply and use of blood and blood components in Europe 2017, 2018 and 2019 report, revised edition was published in 2025

The collection, supply and use of blood and blood components in Europe 2020-2023 report was published in 2025 (5). In addition to the above, a report was published in 2023, providing an overview of the vCJD deferral criteria applied to blood donation in European countries together with perspective on relevant policy changes foreseen in this regard.

Blood Quality Management Programme

The B-QM Programme is aimed at supporting European blood establishments (BEs) in developing, implementing and improving their Quality Management System (QMS) (6). It also takes into account the specificities of the blood transfusion field. The B-QM Programme is an assistance and educational programme delivering virtual / on-site training and assessment schemes open to BEs from the European Union and Council of Europe member states. B-QM Activities include on-site and virtual schemes: Blood Tailored Expert Support (B-TES), is offered in virtual format and aims to prove tailored support to the staff of the requesting BE on technical and / or QMS issues raised prior to the scheme, and recommendations on how to address these issues from a quality management perspective; Blood Training Visit (B-TV) which starts with a visit to the BE, and issues encountered by the BE and non-compliances observed during the visit are collected and training is then provided to BE staff on technical and QMS topics, Blood Mutual Joint Visit (B-MJV)s are intended to advise the BEs and help them implement and / or improve their QMS. The QMS under development in the BE is observed and recommendations are provided. There is Mutual Joint Audit (B-MJA), as well, which is intended to check that the QMS implemented in the BE complies with the requirements of the standards and regulations to be followed (minimum standards used: EU Blood legislation and Council of Europe's *Guide to the preparation, use and quality assurance of blood components*). As of 2022, B-MJAs, B-MJVs and B-TVs can be offered in virtual format as an alternative to the on-site schemes. All schemes are carried out by peers, experts from European BEs, who provide and share their experience and knowledge.

As part of the B-QM Programme, the EDQM also organises training courses and conferences on Quality Management with the aim of sharing best practices in the blood transfusion field. One of the examples was very successful EDQM Blood Conference: Innovation in blood establishments held in January 2025 in Strasbourg, attended by more than 250 international participants (7,8). This conference was an opportunity to engage with the blood sector's international community of experts, to present cutting-edge research, share expertise and discuss practical aspects and challenges.

Blood Proficiency Testing Scheme (B-PTS) Programme

The purpose of the Blood Proficiency Testing Scheme (or B-PTS) programme is to improve the safety of blood components, plasma-derived medicinal products, organs and tissues and cells, and therefore protect patients receiving blood transfusions, undergoing a transplant or benefitting from medically assisted reproduction (9). European Union legislation and the Good Practice Guidelines (GPG) in the Council of Europe's Guide to the preparation, use and quality assurance of blood components and Guide to the quality and safety of tissues and cells for human application require blood testing laboratories to participate in external quality assessment (EQA) initiatives such as PTS programmes, which are also recognised as an important aspect of any quality management system (QMS). Seven B-PTS studies are organised every year. The EDQM designs and organises B-PTS studies according to the principles laid out in ISO/IEC 17043:2023 Conformity assessment – General requirements for the competence of proficiency testing providers. This initiative has been assisting European blood establishments since 2010 and, since 2025, laboratories performing testing on living organ, tissue and cell donors. It is co-funded by the EDQM and the European Commission.

All European laboratories responsible for the testing of SoHO donors in Council of Europe member states may participate in B-PTS studies.

In 2026, an average of 69 laboratories participated in each B-PTS study, covering 39 countries from the Council of Europe and European Union. The 7 B-PTS studies carried out in 2025/26 were:

B-PTS081 Bacterial testing of platelet components

B-PTS082 HBV/HCV/HIV NAT

B-PTS083 Anti-HCV

B-PTS084 HBsAg/Anti-HBc

B-PTS085 Anti-Treponema

B-PTS086 Anti-HIV/p24

B-PTS087 ABO Rhesus, extended phenotyping and irregular antibodies

Blood Supply Contingency and Emergency Plan

Contingency planning and emergency preparedness are key elements of a national blood system. It is vital to ensure that when faced with emergencies a safe and adequate supply of blood can be maintained and made available for all essential transfusions. As part of its co-operation with the European Commission, the EDQM co-ordinated the Blood Supply Contingency and Emergency Plan (B-SCEP) Project (10). It aimed to strengthen national plans to ensure continuity of the blood supply in emergency situations, developing strategies to support European countries in this regard. In 2022, recommendations and a model preparedness plan were published, from which action and mitigation plans based on the overall impact on the blood supply can be tailored accordingly, to accommodate individual blood systems.

Plasma Supply Management

The EDQM continues to help strengthen the implementation of measures to promote and support safe plasma donation and donor protection, and to ensure continued and safe access for patients to plasma-derived medicinal products for life-saving treatments.

The EDQM convened a stakeholder event on “Plasma Supply Continuity” in Strasbourg on 26–27 March 2025 (11). More than 160 representatives of blood establishments, plasma fractionators, patient and donor organisations, industry, regulators, academia, and European institutions updated and reviewed the current state of plasma supply, shared good practices, and discussed actions to increase and improve plasma collection in Europe and secure sustainable access to PDMPs for patients. This major stakeholder event brought together key actors from across Europe to identify priorities and define practical action to support plasma supply continuity. The outcomes of this work are informing ongoing and future initiatives, including the development of policy recommendations and technical guidance to support member states in securing sustainable plasma and PDMP supply. Report was published afterwards which summarises the discussions and outcomes of the Strasbourg meeting. It is intended to inform member states and other stakeholders, providing the key updates and discussion points, highlighting the key priorities set out above, and underscoring the need for action and further support.

Similar Plasma Supply Management Symposium, was jointly organised by the EDQM and the European Commission in January 2019, discussed the facts and scientific evidence surrounding the collection of plasma for fractionation and the elaboration of donor eligibility criteria to ensure donor protection (12). Based on the outcomes of the symposium a set of recommendations were published which represent actions to be undertaken by different stakeholders in order to increase the availability of plasma for fractionation in Europe.

Specifically in relation to plasma, derived Anti-D Immunoglobulin, the EDQM hosted a series of webinars in 2023 to raise awareness on the challenges in the collection of anti-D plasma, the production of plasma-derived anti-D IgG products and to explore potential solutions including the development and use of alternative and complimentary anti-D products. Report on anti-D plasma collection was produced in 2026 (13). It focuses on scientific, technical, regulatory and operational considerations to support the development of European anti-D plasma collection programmes. The aim is to inform and support the (re-)establishment of co-ordinated, sustainable anti-D plasma collection efforts across European member states. Ensuring a secure and sustainable supply of anti-D immunoglobulin is essential to protect maternal and neonatal health across Europe.

Activity Data Set for Blood and Blood Components

The EDQM, in collaboration with the European Commission (DG SANTE), is co-ordinating a project to define a minimum activity data set for blood and blood components, in line with Article 41 of the EU SoHO Regulation (14). A standardised minimum activity data set can serve as a common reference point for stakeholders and authorities, and form the foundation for more structured and reliable data collection and reporting for blood and blood components in Europe – with the objective to support donor and recipient protection, monitor the sufficiency of blood and plasma supply, promote transparency and oversight of activities, and minimise duplication while improving efficiency.

Optimal use of blood components and plasma-derived medicinal products

The EDQM has worked on the optimal use of blood components and plasma-derived medicinal products (PDMPs) since the 1990s. It organises regular symposia – known as the Kreuth Initiatives – which provide a unique platform for exchanging and discussing current clinical practices and projections of future developments across European member states. From these symposia, recommendations and/or legal instruments are developed, which aim at providing a course of action to stakeholders and decision makers in the field to contribute to optimal use and to achieving a higher degree of self-sufficiency. The proceedings from Kreuth Initiative V on the optimal treatment of haemophilia were published as well (15).

Conclusion

The EDQM of the Council of Europe perform a number of activities in the area of blood transfusion guided by the principles of promoting voluntary, non-remunerated blood donation, mutual assistance, optimal use of blood and blood components, and protection of both donor and recipient. The ultimate aim is to ensure the quality, safety and efficacy of blood and blood components and their optimal use, to increase their availability and avoid wastage in maintaining a continuity in their supply.

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Introduction lecture / Uvodno predavanje UV4

QUALITY INDICATORS IN TRANSFUSION MEDICINE: A THREE-YEAR ANALYSIS

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Abstract

Quality indicators (QIs) are essential tools for monitoring performance, ensuring donor and patient safety, and supporting continuous quality improvement in transfusion medicine.

To analyze key quality indicators at the Institute for Transfusion Medicine of the Republic of North Macedonia from 2023 to 2025 and to evaluate trends in donor management, blood collection, blood component quality and wastage.

Materials and Methods: A retrospective observational study was conducted using data extracted from the e-Delphyn blood establishment computer system. Twelve QIs related to donors, collection and blood components were analyzed. Statistical comparisons between 2023 and 2025 were performed using chi-square tests, with $p<0.05$ considered significant.

A total of 175,121 successful donations were recorded. The proportion of first-time donors decreased from 15.5% to 13.5% ($p<0.001$), while the overall donor deferral rate increased from 6.7% to 7.6% ($p<0.001$). Significant improvements were achieved in reducing failed collections (1.7% vs. 1.4%, $p<0.001$), inadequate collection volume (2.6% vs. 0.9%, $p<0.001$), donor adverse reactions (1.7% vs. 1.4%, $p<0.001$), hemolysis (0.08% vs. 0.04%, $p=0.008$) and damaged blood components (1.3% vs. 0.5%, $p<0.001$). Lipemic samples remained stable ($p=0.159$). Expired red blood cell concentrates increased slightly (1.4% vs. 1.6%, $p=0.013$). A marked increase in expired platelet concentrates was observed in 2025 (16.0% vs. 4.5%, $p<0.001$), mainly associated with validation of a new five-part blood bag system with integrated in-line leukocyte filtration.

Several key quality indicators improved significantly during the study period, demonstrating enhanced donor safety, collection performance and blood component quality. Continuous monitoring of QIs proved valuable for identifying trends and guiding targeted quality improvement initiatives.

Keywords: Quality indicators; transfusion medicine; quality management.

Background

A comprehensive Quality Management System (QMS) is a fundamental component of modern transfusion medicine (1). Blood establishments are required to maintain strict quality assurance programs that guarantee the safety of donors and recipients, as well as the integrity of blood components and the safety of clinical transfusion processes (2). Within these frameworks, Quality Indicators (QIs) serve as quantifiable metrics that allow for an objective assessment of operational performance, functioning as indispensable building blocks to monitor processes and facilitate continuous quality improvement (3, 4). To standardize these tools globally, the International Society of Blood Transfusion (ISBT) Quality Management Working Party (QM-WP) established and regularly updates a harmonized global framework of performance measures specifically designed for blood establishments and hospital blood banks (5, 6).

The systemic monitoring of donor-related indicators—including recruitment patterns, deferral rates, donor adverse reactions, and phlebotomy collection success—provides critical insights into donor safety and operational effectiveness (7, 8). Concurrently, product-related indicators—such as visual hemolysis, macro-coagulum formation, inadequate collection volumes, component shelf-life expiration, and structural product damage—directly reflect the efficiency of manufacturing, processing, and inventory management workflows (5, 9).

The Institute for Transfusion Medicine of the Republic of North Macedonia routinely monitors these key QIs by extracting data from the e-Delphyn Blood Establishment Computer System (BECS). The regular evaluation of long-term operational trends enables the identification of institutional strengths, early detection of systemic deviations, and implementation of targeted Corrective and Preventive Actions (CAPA) in alignment with national regulations and international quality standards (10).

Aim:

The primary objective of this study was to analyze and evaluate a comprehensive set of key quality indicators (QIs) monitored at the Institute for Transfusion Medicine of the Republic of North Macedonia across a three-year operational period (2023–2025). Specifically, this study aimed to assess longitudinal trends in donor demographic management, phlebotomy and blood collection efficiency, physical blood component quality parameters, and inventory-related component wastage, thereby identifying operational strengths and areas requiring targeted quality interventions.

Materials and Methods

A retrospective, longitudinal observational study was conducted at the Institute for Transfusion Medicine of the Republic of North Macedonia, covering institutional operations from January 1, 2023, through December 31, 2025. As the central national blood establishment, the Institute oversees blood collection, processing, testing and distribution protocols across the country. All operational and clinical metrics were systematically tracked and extracted from the e-Delphyn blood establishment computer system (Hemasoft). The e-Delphyn database provides real-time, validated monitoring of the entire blood supply chain, ensuring high data integrity and traceabilities from initial donor registration to final component disposition. Twelve specific quality indicators were selected and analyzed in accordance with national guidelines and international hemovigilance recommendations. Annual percentages and a three-year mean were calculated for each quality indicator. To evaluate operational trends, statistical comparisons were performed between the baseline year (2023) and the final year (2025). Proportions were analyzed using the Pearson chi-square (χ^2) test. All statistical tests were two-tailed, with significance set at $p < 0.05$.

Results

1. Blood Donor Demographics and Deferral Dynamics

Over the three-year observation period, total donor numbers evaluated for eligibility increased progressively from 60,499 in 2023 to 65,216 in 2025 (Table 1). Concurrently, a significant downward shift was observed in the influx of new donors; the percentage of first-time blood donors fell from 15.5% to 13.5% ($p < 0.001$; Table 2). This change was accompanied by a statistically significant upward trajectory in the overall donor deferral rate, which climbed from 6.7% in 2023 to 7.6% in 2025 ($p < 0.001$). Interestingly, while low hemoglobin levels remained the primary cause of donor exclusion—maintaining a steady 3-year mean of 3.7%—the slight absolute increase from 3.6% to 3.8% did not reach statistical significance ($p = 0.088$). This indicates that other, non-hemoglobin selection criteria drove the rising deferral trend.

2. Phlebotomy and Collection Efficiency

Operational performance metrics at the collection site demonstrated highly significant quality improvements. Phlebotomy-related complications decreased across the board. Failed collections dropped from 1.7% in 2023 to 1.4% in 2025 ($p < 0.001$). Similarly, instances of inadequate collection volumes of whole blood were drastically mitigated, dropping from 2.6% to 0.9% ($p < 0.001$). Enhanced donor care was reflected in a significant reduction of donor adverse reactions and medical complications during or immediately following phlebotomy, which fell from 1.7% to 1.4% ($p < 0.001$).

3. Blood Component Quality and Processing Specifications

Indicators monitoring component preparation and processing integrity yielded mixed findings. Physical preservation metrics showed favorable shifts; visual hemolysis detected in blood components was cut in half, dropping from 0.08% to 0.04% ($p = 0.008$). Furthermore, the optimization of component manipulation and centrifugation workflows led to a major reduction in physically damaged blood components, decreasing from 1.3% to 0.5% ($p < 0.001$). Conversely, macroscopic coagulums detected within red blood cell (RBC) concentrates experienced a subtle but statistically significant increase from 0.02% to 0.04% ($p = 0.038$). The proportion of lipemic donations remained statistically unchanged across the years, hovering around a 3-year mean of 2.3% ($p = 0.159$).

4. Component Wastage Profiles

Component storage management and expiration trends showed the most pronounced fluctuations during the study period. Storage losses due to expired RBC concentrates underwent a small but statistically significant increase from 1.4% in 2023 to 1.6% in 2025 ($p = 0.013$), despite an exceptional reduction to 0.2% during the interim year of 2024.

The most critical operational deviation occurred within platelet inventory management. Platelet concentrate expiry rates escalated drastically from 4.5% in 2023 to 16.0% in 2025 ($p < 0.001$). This pronounced trend inversion in 2025 directly correlated with institutional infrastructure changes, specifically the extensive validation and operational roll-out of a new five-part blood bag system featuring integrated in-line leukocyte filtration elements.

Table 1. Quality indicators in donor selection, blood collection and blood component management (2023–2025)

Quality Indicator	2023 N/Ntotal (%)	2024 N/Ntotal (%)	2025 N/Ntotal (%)	3-Year Mean %
First-time donors	8770/56450 (15.5%)	8284/58438 (14.2%)	8157/60233 (13.5%)	**14.4%**
Deferral donor rate – total	4049/60499 (6.7%)	4258/62696 (6.8%)	4983/65216 (7.6%)	**7.0%**
Donor deferral due to low hemoglobin	2193/60499 (3.6%)	2396/62696 (3.8%)	2483/65216 (3.8%)	**3.7%**
Failed collections	967/56450 (1.7%)	762/58438 (1.3%)	838/60233 (1.4%)	**1.5%**
Coagulums in RBC concentrates	12/56450 (0.02%)	20/58438 (0.03%)	26/60233 (0.04%)	**0.03%**
Inadequate volume of whole blood collected	1451/56450 (2.6%)	508/58438 (0.9%)	521/60233 (0.9%)	**1.5%**
Donor adverse reactions / complications	936/56450 (1.7%)	728/58438 (1.2%)	838/60233 (1.4%)	**1.4%**
Hemolysis	45/56450 (0.08%)	37/58438 (0.06%)	25/60233 (0.04%)	**0.06%**
Lipemic samples	1258/56450 (2.2%)	1543/58438 (2.6%)	1270/60233 (2.1%)	**2.3%**
Expired PLT concentrates	796/33638 (4.5%)	267/34807 (0.8%)	6121/38177 (16.0%)	**7.1%**
Expired RBC concentrates	777/54993 (1.4%)	94/61501 (0.2%)	1059/66746 (1.6%)	**1.1%**
Damaged blood components	1969/146775 (1.3%)	810/159213 (0.5%)	781/170326 (0.5%)	**0.77%**

Table 2. Statistical comparison of quality indicators between 2023 and 2025

Quality Indicator	2023 (%)	2025 (%)	p-value
First-time donors	15.5	13.5	<0.001
Total donor deferrals	6.7	7.6	<0.001
Low hemoglobin deferrals	3.6	3.8	0.088
Failed collections	1.7	1.4	<0.001
Coagulums in RBC concentrates	0.02	0.04	0.038
Inadequate collection volume	2.6	0.9	<0.001
Donor adverse reactions	1.7	1.4	<0.001
Hemolysis	0.08	0.04	0.008
Lipemic samples	2.2	2.1	0.159
Expired platelet concentrates	4.5	16.0	<0.001
Expired RBC concentrates	1.4	1.6	0.013
Damaged blood components	1.3	0.5	<0.001

Discussion

The longitudinal evaluation of Quality Indicators (QIs) at the Institute for Transfusion Medicine of the Republic of North Macedonia from 2023 to 2025 demonstrates the dynamic interplay between technological modernization, donor demographics, and operational workflows. Tracking these metrics over a three-year span provides a reliable mechanism to measure quality improvements and isolate systemic disruptions that require corrective actions (1,4,5,6).

Donor Demographics and Deferral Trajectories

A primary concern highlighted by our data is the statistically significant decline in first-time donors, dropping from 15.5% to 13.5% ($p < 0.001$). This trend mirrors a widespread global challenge in contemporary transfusion medicine, where blood establishments struggle to recruit and retain younger or new-generation donors (11). Concurrently, the overall donor deferral rate experienced a significant increase, rising from 6.7% to 7.6% ($p < 0.001$). While low hemoglobin levels remained the leading clinical cause of donor exclusion—maintaining a stable three-year mean of 3.7% without significant annual variation ($p = 0.088$)—the rise in total deferrals must be attributed to non-hemoglobin selection criteria. This up-

ward shift likely reflects a stricter adherence to updated donor selection questionnaires, more rigorous pre-donation screening protocols, or evolving regional epidemiological deferral factors aimed at safeguarding the blood supply chain (4,12).

Major Advancements in Phlebotomy and Processing Quality

In contrast to donor recruitment challenges, the Institute achieved remarkable quality improvements in phlebotomy and component manufacturing efficiency. Failed collections decreased from 1.7% to 1.4% ($p < 0.001$), while instances of inadequate whole-blood collection volumes saw a major reduction from 2.6% to 0.9% ($p < 0.001$). Minimizing under-filled or inadequate collections is crucial, as low-volume units directly lead to the automatic discard of both plasma and red cell components due to skewed anticoagulant-to-blood ratios (9). Furthermore, the parallel reduction in immediate donor adverse reactions (1.7% down to 1.4%, $p < 0.001$) underscores enhanced phlebotomist training, better pre-donation hydration counseling and improved donor care protocols (8).

Component processing quality similarly advanced. Visual hemolysis was halved (0.08% to 0.04%, $p = 0.008$), and damaged blood components fell significantly from 1.3% to 0.5% ($p < 0.001$). These improvements demonstrate that processing workflows—such as centrifugation parameters, automated separation steps, and component handling—became highly optimized over the three-year study period (9). However, a small but statistically significant rise in macroscopic coagulums within RBC concentrates (0.02% to 0.04%, $p = 0.038$) was observed. Although the absolute numbers remain very low, this subtle increase warrants continued monitoring and may point to occasional variations in initial mixing techniques during phlebotomy or minor variations in early anticoagulation dynamics (1).

The Technological Impact on Platelet Wastage

The most profound operational deviation observed during the study period was the drastic escalation in expired platelet concentrates, which surged from 4.5% in 2023 to 16.0% in 2025 ($p < 0.001$). This sharp rise in component wastage represents a classic "technology transition phase" disruption. In 2025, the Institute undertook the extensive validation and operational roll-out of an advanced five-part blood bag system featuring integrated in-line leukocyte filtration elements.

While the implementation of this system is a major milestone that directly improves recipient safety by ensuring universal leukoreduction and reducing transfusion-associated adverse reactions (1,10), the initial validation phase introduced severe inventory challenges. During the transition, extensive operational validation protocols required holding numerous platelet units for quality control testing and processing evaluation rather than immediate clinical release. Given that platelet concentrates possess an inherently short shelf-life (typically 5 to 7 days) under continuous agitation, these mandatory validation delays inevitably resulted in a sharp surge in expirations (13). Because this validation phase is currently ongoing and has not yet achieved satisfactory operational outcomes, immediate adjustments to processing workflows and inventory management algorithms are required to synchronize collection volumes with clinical demand and bring platelet expiry rates back to baseline levels (9).

Red Blood Cell Inventory Dynamics

RBC concentrate expiration rates remained well-controlled overall, exhibiting a three-year mean of 1.1%. The significant fluctuation seen in 2024 (dropping down to an exceptional 0.2% before returning to 1.6% in 2025, $p = 0.013$) indicates highly responsive inventory management during that interim period. The slight increase in 2025 balances out the baseline but highlights the continuous need for robust first-in, first-out (FIFO) logistics and proactive communication with clinical blood banks to minimize the expiration of cross-matched but unused units (9).

Conclusion

The three-year longitudinal analysis of quality indicators at the Institute for Transfusion Medicine of the Republic of North Macedonia demonstrates a clear division between phlebotomy performance and inventory adaptation. Significant improvements in failed collections, inadequate volumes, donor adverse reactions, visual hemolysis and component damage confirm that targeted staff training and optimized manufacturing workflows successfully enhanced both donor safety and product processing quality.

Conversely, the significant decline in first-time donors combined with rising overall deferrals highlights an immediate need for modernized public recruitment and donor retention strategies. The most critical operational challenge identified was the sharp surge in expired platelet concentrates to 16.0% in 2025. This spike was driven by the introduction of a new five-part blood bag system with integrated in-line leukocyte filtration. Because this validation phase remains ongoing and has not yet achieved satisfactory operational outcomes, it presents a vital opportunity for quality improvement.

Resolving this trend will require immediate adjustments to production schedules, optimized quality control sampling timelines and dynamic inventory algorithms to balance manufacturing processes with clinical demand. Ultimately, this study demonstrates that routine monitoring of quality indicators is an indispensable tool for identifying systemic vulnera-

bilities, evaluating the impact of technological transitions and guiding corrective and preventive actions to safeguard the regional blood supply.

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PREAPARATION AND STORAGE OF BLOOD COMPONENTS: A KEY TO SAFE TRANSFUSION

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Abstract

The preparation and storage of blood components represent fundamental processes in ensuring the safety, quality, and clinical effectiveness of transfusion therapy. Modern blood processing id based on standardized procedures, comprehensive quality management systems, Good Manufacturing Practice (GMP), international recommendations and national Law on Transfusion Medicine providing full traceability and consistent product quality. A unified information system and ISBT 128 labeling standard ensure accurate identification, complete traceability, efficient inventory management and improved patient safety throughout the transfusion chain. Automation has significantly enhanced blood component processing by reducing human errors, improving standardization, incrasing productivity and preserving the biological quality of red blood cells, plasma and platelets. Universal pre-storage leukoreduction has become an essential safety measure, reducing febrile non-hemolytic transfusion reactions, cytomegalovirus transmission, HLA alloimunization and transfusion-related immunomodulation. Pathogen reduction technologies provide an additional layer of protection against known and emerging transfusion-transmitted infections by inactivating a broad spectrum of viruses, bacteria and protozoa while maintaining the therapeutic function of blood components. Furthermore, modern additive solutions for red blood cells and platelets preserve cellular metabolism, extend storage time, improve post-transfusion efficacy and reduce adverse transfusion reactions. The integration of these advanced technologies has transformed contemporary transfusion medicine, ensuring safer blood products, greater operational efficiency, regulatory compliance and improved clinical outcomes of transfused patients.

Key words: transfusion safety, blood components, automation, leukoreduction, pathogen reduction

Sažetak

Priprema i skladištenje krvnih komponenti predstavljaju osnovu u obezbeđivanju bezbedne i efikasne transfuzione terapije. Savremena transfzijska medicina zasniva se na primeni standardizovanih procedura, sistema upravljanja kvalitetom, principa Dobre proizvodjačke prakse (GMP), međunarodnim preporukama i nacionalnom Zakonu o transfuzionoj medicini, čime se obezbeđuje potpuna sledljivost i konzistentan kvalitet proizvoda. Jedinstveni informacioni sistem i međunarodni standard obeležavanja ISBT 128 omogućavaju preciznu identifikaciju, potpunu sledljivost svake jedinice krvi, efikasno upravljanje zalihama i poboljšanu bezbednost pacijenata u celom lancu transfuzije. Automatizacija procesa pripreme krvnih komponenti značajno doprinosi standardizaciji postupaka, povećava efikasnost rada, smanjuje uticaj ljudskog faktora i obezbeđuje ujednačen kvalitet eritrocita, trombocita i plazme. Univerzalna predepozitna leukoredukcija postala je značajna mera povećanja bezbednosti transfuzije, smanjujući rizik od febrilne nehemolitičke transfuzione reakcije, prenos citomegalovirusa, HLA aloimunizaciju i imunomodulaciju izazvanu transfuzijom. Tehnologije inaktivacije patogena pružaju dodatni nivo zaštite od poznatih i novih infekcija koje se prenose transfuzijom inaktivacijom širokog spektra virusa, bakterija i protozoa, uz održavanje terapijske funkcije komponenti krvi. Savremeni aditivni rastvori za skladištenje eritrocita i trombocita čuvaju ćelijski metabolizam, produžavaju vreme skladištenja, poboljšavaju efikasnost nakon transfuzije i smanjuju neželjene transfuzijske reakcije. Primena ovih naprednih tehnologija transformisala je savremenu transfuzijsku medicinu, obezbeđujući bezbednije krvne komponente, veću operativnu efikasnost, usklađenost sa propisima uz unapređenje ishoda lečenja i povećanje bezbednosti pacijenata.

Ključne reči: bezbednost transfuzije, komponente krvi, automatizacija, leukoredukcija, inaktivacija patogena

Component transfusion therapy involves the administration of specific blood components to patients in order to restore and maintain normal physiological functions. This therapeutic approach improves circulating blood volume, oxygen-carrying capacity, hemostatic function, and immune regulation by replacing only the deficient blood component. Consequently, it minimizes the risk of circulatory overload and reduces unnecessary exposure to blood cell antigens and plasma proteins (1).

The preparation of blood components is governed by national regulations, international recommendations, and comprehensive quality management systems designed to ensure the safety, efficacy, and consistency of blood products. The principles of Good Manufacturing Practice (GMP), originally developed for the pharmaceutical industry, have been adopted in transfusion medicine to guarantee standardized production, processes, product traceability and continuous quality improvement. Current blood component processing is performed in accordance with Guide to the preparation, use and quality assurance of blood components of the European Directorate for the Quality of Medicines and HealthCare (EDQM), supported by validated Standard Operating Procedures (SOPs) that define every stage of collection, processing, testing, storage and distribution. In the Republic of Serbia, the Law on Transfusion Medicine, adopted in 2017, provides the legal framework governing transfusion activities and ensuring the quality and safety of blood and blood components. Licensed blood establishments are required to implement and maintain quality management systems that comply with applicable national legislation and European Union directives. All procedures must be standardized, documented, regularly validated and performed by appropriately trained and qualified personnel. Electronic documentation and validated information system further enhance process control, data integrity and traceability. Regulatory authorities oversee compliance with these standards through routine inspections, ensuring that blood components are prepared and handled according to established quality and safety requirements. A robust quality management system is essential for maintaining the integrity of blood components, minimizing risks throughout the transfusion chain, and ensuring optimal patient safety (1, 2).

Unified information system and labeling of blood components

A unified information system is essential for ensuring the safety, quality, efficiency and traceability of blood and blood components. It ensures complete traceability of every blood unit throughout processing and storage, supports accurate identification and labeling of blood units and blood components, monitors and documents all processing steps, including centrifugation, component separation, leukoreduction, irradiation and pathogen reduction, records the time, date, equipment and personnel involved in each processing procedure and enables continuous monitoring of storage conditions, including temperature, storage location and expiration dates. Also it prevents the release or transfusion of expired, quarantines or non-conforming blood components, facilitates inventory management by tracking stock levels, availability and distribution, reduces human errors through automation and barcode-based identification, ensures compliance with GMP, ISO standards and national transfusion regulations, supports quality control and quality assurance by maintaining complete electronic records and audit trials, enables rapid recall of blood components if quality or safety issues are identifies,improves operational efficiency, reduces waste, optimizes the utilization of blood products and provides reliable data for hemovigilance, audits, accreditation an continuous quality improvement (3).

ISBT 128 is the international recognized standards for the identification, labeling and information transfer of blood, blood components, tissues, cells and organs intended for transplantation. It provides a global unique identification system that ensures complete traceability and enhances patient safety throughout the transfusion chain. By providing standardized identification, accurate labeling and complete traceability, it minimizes the risk of transfusion errors, enhance interoperability between blood establishments, hospitals and healthcare systems, enables efficient inventory management and integration with modern laboratory information system. Its global adoption has significantly improved the safety, efficiency and harmonization of transfusion practice worldwide (4).

Automation

Automation in blood processing plays a crucial role in ensuring the safety, quality and efficiency of blood component preparation. Modern automated technologies standardize the separation of whole blood into red blood cells (RBC), fresh frozen plasma (FFP) and platelet concentrates (PC), minimizing human intervention and reducing the possibility of errors. This contributes to a safer and more reliable blood supply for patients. The main advantages of automation include:

- enhanced patient safety by reducing manual handling and the risk of human error during blood component preparation,
- standardized processing, ensuring that every blood unit is prepared under identical, validated conditions, resulting in consistent product quality,
- improved traceability, allowing complete monitoring for each blood unit from donor to recipient and ensuring compliance with international quality standards,
- reduced risk of bacterial contamination through the use of closed systems and minimal manipulation of blood components,
- higher efficiency and productivity, enabling laboratories to process larger numbers of blood units with less labor and shorter turnaround times,
- optimized blood component quality, as automated centrifugation and separation provide better recovery of

RBC, plasma and platelets while preserving their biological function,
- lower variability between operators, leading to reproducible results,
- improved compliance with GMP and SOPs,
- better resource utilization, reducing workload for laboratory personnel and allowing staff to focus on quality assurance and patient care.

All of these improvements ultimately enhance transfusion safety, reduce adverse transfusion reactions and ensure that patients receive blood products of the highest possible quality (5,6).

Leukoreduction

Leukoreduction is a critical step in modern blood component processing, involving the removal of leukocytes from blood products before storage, at the level of $< 5\text{-}10x10^6$ (3 $\log_{10}$ reduction (99,9%)), which significantly improves the safety, quality and clinical effectiveness of transfusion therapy (7). According to AABB (American Association of Blood Banks) standards, the residual number of leukocytes in leukoreduced components must be $< 5x10^6$, while European recommendations require $< 1x10^6$ in 97% of tested units and $< 5x10^6$ in 100% of units (8,9).

Removing leukocytes decreases the release of inflammatory cytokines, thereby reducing the incidence of febrile non-hemolytic transfusion reactions (FNHTRs) and other transfusion-related reactions. Also it reduces risk of cytomegalovirus (CMV) transmission, prevents HLA alloimunization and decreases transfusion-related immunomodulation (TRIM). Universal pre-storage leukoreduction is considered the standard of care in many countries and is recommended by international transfusion medicine organizations as an essential quality and safety measure (10).

Leukoreduction is achieved using sterile, single-use filters specificially designed to selectively retain leukocytes while allowing RBCs, PLTs and plasma to pass through with minimal loss. There are RBC filters, PLT filters, whole blood filters and integrated blood bag systems (in-line).

Pathogen inactivation

Pathogen inactivation (pathogen reduction technology (PRT)) is one of the most significant advances in transfusion medicine. It is a proactive strategy designed to reduce the risk of transfusion-transmitted infections (TTIs) by inactivating a broad spectrum of pathogens- viruses (such as Flaviviruses Den-1-Den-4, St.Louis Encephalitis Virus, Togaviruses of Western and Eastern Equine Encephalitis, Chikungunuya, Respiratory Corona Viruses, Circovirus TT and SEN, Deltavirus Hepatitis D, Epstein-Barr Virus, Human Herpes Viruses 6, 7 and 8, Parvovirus B19), bacteria (Stapylococcus aureus, Stapylococcus epidermidis, Escherihia colli, Anaplasma phagocytophilum, Borelia burgdoferi), protozoa (Babesia microti, Toxoplasma gondii, Trypanosoma cruzi, Leischmania donovani) or prions (cause Creutzfeldt-Jakob disease). Unlike donor screening of TTIs, which identify only known pathogens, PRT provides an additional layer of safety against both known and emerging infectious agents (11).

Most PRTs target the nucleic acids (DNA and RNA) of microorganisms by preventing replication, pathogens lose their ability to infect recipients while preserving the therapeutic function of blood components. The process generally involves addition of photosensiting agent (amotosalen, riboflavin), exposure to ultraviolet light, cross-linking or irreversible damage to nucleic acids and elimination or neutralization Since mature RBCs do not contain nuclei and platelets have limited nucleic acid activity, these treatments can effectively inactivate pathogens while maintaining acceptable blood component quality. But, developing PRT for RBCs is more challenging because hemoglobin absorbs UV light and RBCs are highly sensitive to oxidative damage (12).

Routine implementation of PRT reduces the risk of TTIs, provides protection against newly emerging pathogens, significantly decreases bacterial contamination of PCs, inactivates residual donor leukocytes, reducing the risk of transfusion-associated graft-versus-host disease (TA-GVHD) and improves the overall safety of the blood supply. Despite its benefits, PRT has certain limitations, such as additional processing costs, potential reduction in PLT recovery and function, limited availability of licensed technologies for RBCs and requirement for specialized equipment and staff.

Additive solutions for Red Blood Cells and Platelets storage

Additive solutions are specially formulated preservation media used during the preparation and storage of blood components. Their primary purpose is to maintain cell viability, functionality and metabolic activity while extending shelf life and improving transfusion safety. Modern additive solutions have become an essential component of blood processing and are widely used in conjuction with automated blood component preparation, leukoreduction and PRTs (13).

RBC additive solutions (RAS) are designed to preserve RBCc after plasma removal by providing nutrients and main-

taining cellular metabolism during storage (2-6°C). They maintain ATP production, preserve 2,3-DPG levels, stabilize the red cell membrane, reduce hemolysis, improve post-transfusion red cell survival and extend storage to 42 days. Although formulations differ slightly, most RAS contain saline, adenine, glucose (dextrose), manitol and citrate or phosphate. The most common RASs are SAGM, AS-1, AS-3, AS-5 (14).

Platelet additive solutions (PAS) partially replace donor plasma and are used to store PCs while maintaining platelet function. PCs are stored at 20-24°C with continuous agitation for up to 5-7 days, depending on national regulations and bacterial risk strategies. PAS reduce plasma volume, decrease allergic transfusion reactions, lower the risk of ABO incompatibility, improve platelet storage quality, faciliate PRT, preserve platelet metabolism and reduce citrate exposures in recipients. Most PAS contain sodium chloride, sodium acetate, sodium citrate, potassium chloride, magnesium chloride and phosphate buffers. Acetate serves as an alternative metabolic substrate, helping maintain platelet energy production and pH. Common PASs are PAS-B, PAS-C, PAS-E (SSP+) and PAS-F. PAS help maintain platelet count, swirling phenomenon, pH>6,4, low lactate accumulation, adequate glucose consumption, platelet morphology and platelet aggregation and function (15).

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APPLICATION OF THE MEDIVEN® SET IN THE PREPARATION OF AUTOLOGOUS SERUM EYE DROPS

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Abstract

Autologous serum eye drops represent an important therapeutic option for ocular surface diseases, particularly in patients with severe dry eye syndrome. The aim of this study was to evaluate the safety and effectiveness of the MedEnvy set for standardized preparation of autologous serum eye drops in a transfusion medicine setting.

A retrospective study was conducted at the Transfusion Center of the University Clinical Hospital Mostar (2022–2025) using data from the hospital information system (BIS), medical documentation, and laboratory records.The analysis included 61 patients, 103 procedures, and 295 prepared autologous serum sets. The most common indication was dry eye associated with autoimmune diseases. Complications were rare and no serious adverse events were recorded. Approximately 75% of patients reported subjective and clinical improvement in symptoms. The MedEnvy set enabled standardized, safe, and reproducible preparation of autologous serum eye drops.

The MedEnvy set is a safe and effective system for routine clinical preparation of autologous serum eye drops.

Keywords: autologous serum; dry eye; transfusion medicine.

Sažetak

Autologni serum predstavlja suvremenu terapijsku opciju u liječenju bolesti površine oka, posebno kod pacijenata sa teškim oblicima sindroma suhog oka. Cilj ovog rada bio je procijeniti sigurnost i efikasnost primjene MedEnvy seta u standardiziranoj pripremi autolognih serumskih kapi u uslovima transfuzijske medicine.

Provedena je retrospektivna studija u Transfuzijskom centru SKB Mostar (2022.–2025.) koristeći podatke iz bolničkog informatičkog sustava (BIS), medicinske dokumentacije i laboratorijskih zapisa. U analizu je uključeno 61 pacijent, 103 postupka i ukupno 295 pripremljenih setova autolognog seruma. Najčešća indikacija bila je suho oko u sklopu autoimunih bolesti. Procjenjivani su klinički ishodi i eventualne komplikacije tokom pripreme i primjene. Komplikacije su bile rijetke i bez ozbiljnih neželjenih događaja. Kod približno 75% pacijenata zabilježeno je subjektivno i kliničko poboljšanje simptoma. MedEnvy set omogućio je standardiziranu, sigurnu i reproducibilnu pripremu autolognih serumskih kapi.

MedEnvy set predstavlja efikasan i siguran sistem za pripremu autolognog seruma u rutinskoj kliničkoj praksi.

Ključne riječi: autologni serum; suho oko; transfuzijska medicina

Introduction

Ocular surface diseases represent a heterogeneous group of disorders involving the tear film, conjunctiva, and cornea, and are increasingly recognized as a significant public health and clinical concern due to their chronic course and substantial impact on patients' quality of life (1, 2). Dry eye syndrome is the most common entity within this group and is characterized by tear film instability, increased tear osmolarity, and chronic inflammation of the ocular surface, leading to symptoms such as burning sensation, foreign body sensation, blurred vision, and photophobia (1-5).

Particularly severe forms of dry eye syndrome occur in patients with autoimmune diseases, including Sjögren's syn-

drome, rheumatoid arthritis, and systemic lupus erythematosus, where immune-mediated destruction of the lacrimal glands results in significant tear secretion deficiency and progressive damage to the ocular surface (1, 2). In such cases, standard therapy, including artificial tears, lubricants, topical anti-inflammatory agents, and immunomodulators, is often insufficient to achieve adequate symptom control and preserve epithelial integrity (3, 5).

Over the past decades, biological therapy has gained increasing importance, with autologous serum occupying a prominent place as a natural, patient-tailored therapeutic approach. Autologous serum contains numerous biologically active components, including growth factors (epidermal growth factor and fibroblast growth factor), vitamins, fibronectin, lysozyme, and other proteins that are structurally and functionally similar to the components of the natural tear film, thereby contributing to regeneration, epithelial healing, and reduction of ocular surface inflammation (3, 6, 7, 8).

Unlike commercially available artificial tears, autologous serum represents an individualized biological preparation derived from the patient's own blood, thereby reducing the risk of immunological reactions and increasing the biocompatibility of the therapy. However, its clinical application requires strict standardization of preparation, storage, and quality control procedures in order to ensure safety and reproducibility of the therapeutic effect (6, 7).

In this context, transfusion medicine plays a crucial role by enabling the controlled preparation of biological products in accordance with the principles of aseptic technique, laboratory quality control, and biosafety. Contemporary approaches also include microbiological monitoring of the preparations, encompassing the detection of aerobic and anaerobic bacterial flora, as well as fungal contaminants, thereby further ensuring the safety of autologous serum application in clinical practice (6, 7, 9).

The MedEnvy set represents an advanced system for the closed and standardized preparation of autologous serum eye drops, enabling reduced variability in the preparation process, minimization of contamination risk, and improved reproducibility of the final product. Its implementation within transfusion centers contributes to the development of the concept of "hospital-based biologics production" in which patient-tailored therapy is produced within a controlled hospital environment (6–8).

Objective

The aim of this study was to evaluate the safety, clinical efficacy, and practical applicability of the MedEnvy set in the preparation of autologous serum eye drops within routine transfusion medicine practice.

Particular emphasis was placed on the significance of enabling the standardized production of autologous serum within a transfusion center as an individualized biological therapy for patients with severe ocular surface diseases. This approach represents an important advancement in the development of personalized medicine, as it allows the availability of biologically active, safer, and patient-tailored therapy within a controlled hospital-based system.

Materials and methods

A retrospective observational study was conducted at the Transfusion Center of the University Clinical Hospital Mostar during the period from January 2022 to December 2025.

The study included patients for whom therapy with autologous serum eye drops was indicated due to ocular surface diseases. Data were obtained from the Hospital Information System (BIS) of the University Clinical Hospital Mostar and collected from medical records, transfusion protocols, and laboratory documentation.

The analyzed parameters included:

- demographic characteristics of the patients
- primary diagnosis and indication for therapy
- number of venipuncture procedures performed
- number of prepared autologous serum sets
- technical and biological complications
- subjective clinical response

Preparation of autologous serum was performed using a standardized protocol with the MedEnvy set, while strictly adhering to aseptic procedures in accordance with transfusion medicine standards.

Results

During the analyzed period, a total of 61 patients were included, in whom 103 autologous blood collection procedures were performed. Demographic distribution demonstrated a marked predominance of female patients (N=44; 72%) compared to male patients (N=17; 28%), with a mean patient age of 60 years. Analysis of the annual number of procedures revealed a continuous increase: 7 procedures were performed in 2022, 17 in 2023, 46 in 2024, and 33 procedures were recorded in 2025.

Based on the collected samples, a total of 295 autologous serum sets were prepared. The most common indication was

dry eye syndrome associated with autoimmune diseases (N=30), while other indications included ocular infections (N=22), traumatic lesions (N=2), status post corneal transplantation (N=1), and other idiopathic or postoperative conditions (N=6). Most patients were referred for therapy by ophthalmologists (38) and immunologists (23).

During the preparation process, only minimal technical difficulties without clinical significance were recorded, including a single unsuccessful venipuncture due to poor venous access. Of the total number of produced sets, two were discarded because of serological reactivity (HBV and syphilis). No hemolysis, contamination, or sample loss during processing was observed. Approximately 75% of patients reported subjective improvement of symptoms, accompanied by objective improvement in tear film stability.

Discussion

The results obtained at the Transfusion Center of the University Clinical Hospital Mostar unequivocally confirm that autologous serum represents a highly effective and safe therapeutic option in the contemporary treatment of complex ocular surface diseases. Its application appears particularly important in patients with severe and refractory forms of dry eye syndrome, in whom standard pharmaceutical preparations fail to achieve a satisfactory clinical response (3, 5, 6). Unlike artificial tears, autologous serum provides biological support that closely mimics the natural tear film.

Its high therapeutic efficacy primarily derives from its rich composition of biologically active components. Serum contains essential growth factors, such as epidermal growth factor (EGF) and transforming growth factor beta (TGF-β), as well as vitamins and fibronectin. These components directly participate in cellular processes that promote ocular surface regeneration, accelerate epithelial healing, and reduce chronic inflammation (3, 6, 8).

In the modern clinical setting, transfusion medicine plays a significant and irreplaceable role in the standardization processes and strict quality control of biological preparations (6–8). The introduction of the MedEnvy set into the routine practice of the University Clinical Hospital Mostar represents an important technological advancement. This system enables a completely closed preparation process, thereby substantially reducing the risk of exogenous contamination and ensuring maximum sterility during the handling of blood and serum (6, 7). Through process standardization using the SCD (Sterile Connecting Device) system, variability of the final product is minimized, ensuring reproducibility of the therapeutic effect.

Our findings regarding subjective and objective clinical improvement in the majority of patients are fully consistent with the available international literature, which confirms accelerated epithelialization and significant improvement in tear film stability following the introduction of this biological therapy (4–6, 8).

This advancement directly contributes to the reduction of distressing symptoms such as burning sensation, foreign body sensation, and photophobia, thereby significantly improving patients' quality of life.

Finally, patient safety is further ensured through strictly controlled testing protocols. Microbiological quality control of each individual preparation, including detailed analysis of aerobic and anaerobic bacterial flora as well as potential fungal contaminants, provides the highest level of biosafety in clinical application (9). Such a comprehensive approach within the Transfusion Center enables autologous serum to become a standard of personalized medicine in the treatment of ophthalmological diseases.

It should be emphasized that this study has certain limitations. The retrospective nature of the study relies on historical data obtained from the Hospital Information System (BIS), which may result in variability in the documentation of subjective symptoms. In addition, the study lacks a control group of patients treated with standard artificial tear therapy, which would allow more precise assessment of the superiority of autologous serum therapy. Future studies should include a prospective design with more precise assessment instruments, such as the OSDI (Ocular Surface Disease Index) questionnaire, in order to quantify improvements in patients' quality of life.

Despite these limitations, the continuous increase in the number of procedures performed at the University Clinical Hospital Mostar during the observed period (from 7 procedures in 2022 to 46 procedures in 2024) clearly indicates high clinical acceptance and a growing need for this method within personalized medicine.

Conclusion

Based on the overall analysis of the study conducted at the University Clinical Hospital Mostar, it can be concluded that the application of the MedEnvy set in the autologous donation process represents a safe, effective, and highly standardized method for the preparation of autologous serum eye drops. The results obtained through analysis of data from the hospital information system for the period from September 2022 to December 2025 confirm that this biological therapy achieves significant success in patients with severe and refractory forms of ocular surface disease, with clinical and subjective improvement observed in approximately 75% of the participants.

The technological advantage of the MedEnvy set is reflected in the establishment of a closed preparation system that minimizes the risk of microbiological contamination and ensures maximum biosafety, which is further supported by the absence of recorded infections during the observed period. The Transfusion Center of the University Clinical Hospital Mostar has proven to be a key component in the implementation of personalized medicine, integrating strict laboratory quality

control and aseptic techniques into the production process of a therapy tailored to the individual needs of each patient.

The minimal number of technical complications and the steady increase in the number of procedures over the years indicate that the system is fully applicable in routine clinical practice and widely accepted by clinicians. In conclusion, the standardized approach provided by the MedEnvy set ensures consistent quality and high therapeutic value of autologous serum, thereby significantly improving the care of patients with the most severe ophthalmological pathologies within the hospital setting.

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PAST AND FUTURE OF ATMP ACTIVITIES IN TRANSFUSION MEDICINE

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Abstract

Advanced Therapy Medicinal Products (ATMPs) include gene therapy medicinal products, somatic cell therapy medicinal products, tissue-engineered products, and combined ATMPs. In broader strategic terms, they belong to the wider field of biotherapies: cellular, gene-modified, tissue-derived, or otherwise biologically active therapies that rely on infrastructures historically developed within transfusion medicine. Blood transfusion was one of the earliest cellular therapies, while hematopoietic stem cell transplantation established many of the operational principles later required for ATMPs, including donor selection, apheresis, compatibility testing, cell processing, cryopreservation, quality systems, traceability, and long-term follow-up. Today, CAR-T cells, virus-specific T cells, mesenchymal stromal cells, dendritic-cell vaccines, gene-edited hematopoietic stem cells, and tissue-engineered products extend this tradition into precision and regenerative medicine.

Across Europe, blood establishments already produce, research, plan, or supply starting material for ATMPs. However, their progress is limited by major barriers such as financing and reimbursement challenges, workforce shortages and training needs, regulatory complexity, and infrastructure constraints. Future strategy should therefore focus on building public national and regional biotherapy hubs around blood, tissue, and cell establishments. These hubs should integrate ethical sourcing, standardized starting material, hospital exemption pathways, GMP-ready manufacturing, workforce development, sustainable reimbursement, registries, accreditation, and cross-border cooperation.

Key words: cellular therapy, immunotherapy, biotherapies

Introduction

In the European Union (EU), ATMPs have a precise legal meaning established by Regulation (EC) No 1394/2007: gene therapy medicinal products, somatic cell therapy medicinal products, tissue-engineered products and combined ATMPs (1). The term biotherapy is broader and includes immune effector cells, cellular starting materials, virus-specific T cells, regenerative products and other living or biologically active therapies. This wider concept is increasingly relevant to transfusion medicine because blood services are involved not only in finished ATMPs but also in the systems that make them possible: donor selection, apheresis, cell processing, cryostorage, quality control, chain of identity and clinical follow-up.

Recent analyses emphasize that biotherapies can offer transformative outcomes in malignant and nonmalignant diseases, but affordability and access require global coordination, interdisciplinary partnership and standardization (2). The strategic problem is therefore no longer only scientific. Manufacturing infrastructure, workforce limitations, starting-material variability, fragmented regulation and high costs can prevent effective therapies from reaching patients.

Historical and scientific continuity

Transfusion is the oldest established cellular therapy. Its reliability followed the discovery of blood groups, compatibility testing, donor screening, component preparation and haemovigilance. Hematopoietic stem cell transplantation then became the first durable cellular therapy in which transferred cells could engraft, proliferate and reconstitute a biological system. It created operational principles that remain essential for ATMPs: donor matching, mobilization, apheresis, cryopreservation, sterility testing, graft characterization, transplant immunology and long-term follow-up (3).

Cellular immunotherapy created a bridge between classical transfusion medicine and immune engineering. Stimulatory therapies include donor lymphocyte infusion, antigen-specific cytotoxic T cells, virus-specific T cells, tumor-infiltrating lymphocytes, genetically modified T cells, NK-cell therapies and dendritic-cell vaccines. Immunomodulatory approaches include regulatory T cells, mesenchymal stromal cells, tolerogenic dendritic cells and extracorporeal photopheresis (4). Many of these products originate from blood, marrow or other substances of human origin and require technologies already embedded in advanced transfusion services.

Current European activity

Blood and tissue establishments are natural participants in ATMP development. They already possess donor-management systems, apheresis expertise, infectious-disease testing, HLA and immunogenetics laboratories, cryobiology, logistics, traceability, biovigilance and GMP-compatible quality systems (5). European practice confirms that the transition is already underway. A survey among European Blood Alliance members showed that several blood establishments already produce ATMPs, others plan or research them, and many supply starting material (6). Reported activities include CAR-T cells, virus-specific T cells, dendritic cells, mesenchymal stromal cells, hematopoietic stem cell therapies, NK cells, Tregs, iPSC-related approaches, keratinocytes, corneal epithelial stem cells, engineered tissues, viral vectors and plasmids. The main barriers were financing, human resources and training, regulatory complexity and infrastructure (6).

The Slovenian experience illustrates a small-country model. The Slovenian Institute for Transfusion Medicine has supported GMP-compliant manufacturing, quality control and clinical use or trials of CD34-positive cell therapy, dendritic-cell vaccines and mesenchymal stromal cell applications (7). European clinical activity is also increasing: the EBMT reported almost 48,000 hematopoietic cell transplant procedures and more than 6,000 advanced cellular therapy treatments in 2023, including nearly 4,900 CAR-T therapies (8). This growth increases pressure on apheresis units, cell-processing laboratories, quality systems, clinical teams and payers.

Why the connection is structural

ATMPs and transfusion medicine are connected at a structural level. They share five core features:

Dependence on substances of human origin. Blood, cells, and tissues are not ordinary raw materials. Their quality depends on donor biology, collection methods, processing time, storage, transport, and documentation.

Reliance on donor and patient trust. Voluntary unpaid donation, donor protection, and public accountability become even more important when donated cells are used for high-value or commercial biotherapies.

Need for full traceability. Both fields require chain of identity, chain of custody, and look-back procedures.

Strong quality systems. Both depend on validated procedures, staff training, deviation management, and inspection readiness.

A personalized-medicine framework. Immunohematology, HLA matching, and patient-specific component support anticipated the individualized logic that now defines many ATMPs.

For many products, starting material is a major determinant of final quality. Autologous cells may be affected by age, disease, chemotherapy exposure, inflammation, lymphopenia, or poor venous access. Allogeneic material depends on donor selection, HLA type, immune history, infectious-disease screening, collection conditions, and cryopreservation. This variability can influence yield, phenotype, expansion, transduction efficiency, potency, and ultimately clinical effect. Harmonized apheresis protocols and quality indicators for cellular starting material should therefore become a core function of transfusion medicine (9).

Legal, ethical and regulatory framework

The ATMP framework allows centralized EU authorization but also recognizes hospital exemption for non-routine, patient-specific preparation under national responsibility (1). Hospital exemption is important for rare diseases, ultra-personalized therapies, small patient populations and academic innovation. It must not become a loophole for unproven interventions, but it should also not be restricted so severely that public-sector development becomes impossible (10).

The new EU Regulation 2024/1938 on substances of human origin is strategically relevant because ATMP manufacturing often begins with SoHO-derived starting material (11). Future policy must define where SoHO activity ends and ATMP manufacture begins, who is responsible for donor eligibility, consent, testing, release, data protection and long-term traceability, and how cross-border exchange is governed. Ethically, blood, cells and tissues should remain public-interest resources grounded in solidarity. Donors must be protected from harm, coercion and inadequate information. Consent should address research, manufacturing, commercialization, storage, data sharing and withdrawal limitations. Public blood establishments should also help protect patients from premature commercialization and unproven “stem-cell” interventions.

Manufacturing, workforce and finance

Industrial manufacturing, decentralized public manufacturing and point-of-care production will probably coexist. Centralized models offer consistency but may create long vein-to-vein times, complex logistics and high prices. Decentralized or point-of-care models may better serve autologous, urgent or hospital-exemption products, but require standardization, qualified staff, release responsibility and regulatory oversight (12).

The workforce bottleneck is equally important. Future programs require trained cell-processing technologists, transfusion physicians, hematologists, pharmacists, qualified persons, quality managers, regulatory scientists, apheresis nurses, clinical-trial coordinators and data managers. Training must include donor eligibility, immune-effector-cell apheresis, asep-

tic processing, cryopreservation, potency testing, deviation management, pharmacovigilance and registry reporting (13).

Financial sustainability cannot be achieved only by negotiating prices. Costs include referral, donor or patient assessment, apheresis, testing, transport, manufacturing, release, hospitalization, toxicity management and long-term follow-up. Shared GMP platforms, regional hubs, accountable public-private partnerships, registries and outcome-based reimbursement can reduce duplication and support access.

Interface with hematology-oncology, EBMT, EHA and JACIE

Cellular therapies are inseparably linked with the hematology-oncology and transplant network. Most established ATMP activity, especially CAR-T therapy, gene-modified hematopoietic stem cells and donor-derived immune effector cells, is clinically delivered through hematology, oncology and transplant programs. Transfusion services provide the operational backbone: donor and patient cell collection, apheresis, starting-material quality, cryopreservation, cell processing, traceability, chain of identity and sometimes GMP manufacturing.

EBMT contributes transplant and cellular-therapy registries, outcome reporting, post-authorization safety data, working parties and European scientific coordination. EHA adds the broader hematology-oncology platform, education, congress visibility and guideline dissemination. JACIE provides the quality bridge between clinical hematology and transfusion/cellular-processing practice; its standards and inspection-based accreditation cover collection, processing and clinical administration of hematopoietic cellular therapies and immune effector cells (14). Future strategy therefore requires an integrated cellular therapy program in which transfusion medicine, hematology-oncology, transplant units, hospital pharmacies, GMP laboratories, registries and accreditation systems function as one coordinated pathway.

Strategy for Serbia and other European countries

Blood establishments should become national and regional biotherapy hubs rather than mere collection sites. Their future role should include autologous and allogeneic starting-material collection, donor registries, apheresis excellence, cell processing, cryopreservation, GMP-ready manufacturing, quality control, HLA and immunogenetics, hospital exemption support, clinical-trial support, regulatory expertise, registries, training and public communication.

A practical strategy for Serbia and other European countries should begin with national ATMP planning. This can be organized into three implementation steps:

Map existing capacity. Assess apheresis capacity, cell-processing laboratories, HLA laboratories, biobanks, cleanrooms, clinical-trial units, transplant centers, regulatory expertise, and reimbursement mechanisms.

Create a national coordination platform. Link the blood service, university hospitals, the medicines agency, ministries, ethics bodies, patient representatives, donor registries, and industry in a shared ATMP/biotherapy framework.

Phase development through public investment. Start with starting-material quality and apheresis, then expand to cryopreservation, quality control, and clinical-trial support, followed by selected non-genetically modified therapies, and later genetically modified products or automated point-of-care manufacturing.

For small and medium-sized countries, regional cooperation is essential. A decentralized but coordinated European model, with blood, tissue, and cell establishments serving as public competence centers, can improve access, reduce duplication, and preserve solidarity-based healthcare (15).

Conclusion

ATMPs and biotherapies are transforming medicine, but their success depends on more than scientific breakthroughs. They require ethical sourcing, standardized starting material, manufacturing capacity, trained personnel, sustainable finance, harmonized regulation, registries and equitable access. These are domains in which transfusion medicine already has deep experience.

The future role of transfusion medicine should therefore be active rather than merely supportive. Blood establishments should not be reduced to apheresis sites for external manufacturers. Instead, they should function as public infrastructures for advanced biological therapy by qualifying starting material, supporting GMP manufacturing, enabling responsible hospital exemption, coordinating registries, training personnel, and protecting donors and patients.

For Serbia and other European countries, the strategic choice must be made now: transfusion medicine can remain a traditional support service, or it can evolve into a central platform for cellular, genetic, regenerative, and immune-based medicine.

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DEVELOPMENT OF HEMATOPOIETIC STEM AND PROGENITOR CELL GRAFTS FROM STEADY-STATE PERIPHERAL BLOOD CD34+ CELLS

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Abstract

Non-mobilized hematopoietic stem cells (HSCs) present in steady-state peripheral blood constitute a rare population within the already limited CD34+ cell pool, yet they possess critical potential for hematopoietic graft development. Our studies demonstrated that CD34+ cells, including this rare HSC fraction, can be efficiently isolated from leukoreduction filters of blood products. These cells also contain functional progenitors capable of proliferating and differentiating into cells of all myeloid lineages. Experiments in immunodeficient mice confirmed that HSCs from homeostatic blood have limited engraftment capacity in the basal state, which is markedly enhanced after ex vivo expansion. Phenotypic and functional analyses revealed a primitive HSC population with high proliferative potential, dependent on low oxygen concentrations and optimized culture conditions with cytokines and small molecules. Ex vivo expansion increases both the number and functional capacity of these rare stem cells, as well as committed progenitors, enabling the development of hematopoietic grafts without prior donor mobilization.

Sažetak

Nemobilisane hematopoetske matične ćelije (HSCs) prisutne u homeostatskoj perifernoj krvi čine retku populaciju i inače retkih CD34+ ćelija, ali imaju ključni potencijal za razvoj hematopoetskih transplantata. Naša istraživanja su pokazala da se CD34+ ćelije, uključujući i ovu retku populaciju HSCs, mogu efikasno izolovati iz leukoredukcijskih filtera krvnih proizvoda. Ove ćelije sadrže i funkcionalne progenitorske ćelije sposobne da proliferišu i diferenciraju se u ćelije svih mijeloidnih loza. Eksperimentima sa imunodeficijentnim miševima potvrđeno je da HSCs iz homeostatske krvi imaju ograničenu sposobnost transplantacije u bazalnom stanju, ali se ona značajno povećava nakon ekspanzije eks vivo. Fenotipske i funkcionalne analize otkrivaju primitivnu populaciju HSCs sa visokim proliferativnim potencijalom, zavisnim od niske koncentracije kiseonika i optimizovanih uslova kulture sa citokinima i malim molekulima. Ekspanzija eks vivo omogućava povećanje broja i funkcionalne sposobnosti ovih retkih matičnih ćelija, a takođe i opredeljenih progenitora, čime se otvara mogućnost koncepcije hematopoetskih transplantata bez prethodne mobilizacije donora.

Introduction

Even before Till and McCulloch in 1961 identified a multipotent progenitor (CFU-S; Colony-Forming Unit-Spleen), experiments on parabiosis between irradiated and normal rats in 1951, later confirmed in baboons, had demonstrated the existence of HSCs (Hematopoietic Stem Cells) capable of reconstituting hematopoiesis in steady-state circulating blood. Long-term hematopoietic reconstitution of irradiated animals after injection of autologous or homologous blood cells definitively proved the persistent presence of these HSCs in the blood under homeostatic conditions (1). Committed progenitors (2) and multipotent progenitors (CFU-S) (3, 4) were also detected in steady-state peripheral blood.

Steady state peripheral HSCs in humans

It should be stressed that long-term transfusion-associated microchimerism, persisting for decades after transfusion of non-leukodepleted blood, provides indirect but compelling evidence that human steady-state peripheral blood contains rare hematopoietic stem cells capable of durable and sustained engraftment. This is especially the case if the recipient was immunosuppressed (5). Similar observations come from studies of maternal microchimerism in the child.

Early clinical trials in the 1980s demonstrated the usefulness of autologous peripheral blood cell transplantation as well as allogeneic transplantation. However, HSPC transplantation is associated with prolonged thrombocytopenia and slow hematopoietic recovery. Their low blood concentration (1–5 CD34+ cells/μL) and the inability at that time to expand

stem cells ex vivo led scientists and clinicians to explore an alternative approach when increased numbers of progenitors and circulating stem cells were observed after chemotherapy and cytokine treatment (GM-CSF or G-CSF), a phenomenon called “mobilization.” Since then, the clinical use has been oriented exclusively to HSPCs mobilized to peripheral blood.

However, some research efforts continued to be invested in steady-state peripheral blood hematopoietic stem and progenitor cells (HSPCs). For example, a French study on the phenotypic and functional characteristics of HSPCs recovered from the leukocyte–platelet layer collected during the preparation of red blood cell concentrates (RBCs) showed that they differ from those derived from bone marrow: they contain more mixed CFUs and CFU-Meg, and there are more erythroid than myeloid progenitors. Primitive LTC-IC (Long-Term Culture Initiating Cells) stem cells were also detected. HSPCs have substantial expansion capacity, which was confirmed in our preliminary experiments (6).

It should also be noted that, unlike bone marrow CD34+ cells, CD34+ cells in homeostatic blood express very little CXCR4 (the receptor for SDF-1) (7), which is essential for the marrow “homing” of hematopoietic stem cells. Short in vitro incubation of CD34+ cells induces CXCR4 expression on their membrane (7), enhancing their in vivo engraftment efficiency.

Although often based on older and limited data, these results suggest that HSPCs from steady-state blood have interesting biological potential. However, the techniques for their collection, preparation, and *ex vivo* manipulation have not yet been sufficiently developed and standardized for application in current cell therapy.

Our contribution to the actualization of steady-state peripheral blood HSC

Our previous research demonstrated the possibility of extracting mononuclear cells from leukoreduction filters of blood products (PSL). Using this initial approach, we obtained approximately 360 million mononuclear cells, including 450, 000 CD34+ cells per leukoreduction filter, and demonstrated that the small fraction of these cells expressing CD34 (around 0.16%) contains functional committed hematopoietic progenitors capable of proliferating and generating mature cells of all myeloid lineages *ex vivo* (6). We further improved the processing of leukocyte-depletion filters (LDF) and recovery of CD34+ cells (8) and provided arguments for their potential usefulness in cell engineering (reprogramming-iPSCs, hematopoietic graft conception, RBC ex vivo production) and pharmaceutical screening (9).

The CD34+ cells from homeostatic blood obtained in this way served as raw material to produce red blood cells ex vivo, by adapting oxygenation during each stage of erythropoiesis. We showed that these variations in oxygenation during culture increased red blood cell production up to fourfold (10). This work also demonstrated that CD34+ cells from adult basal blood perform comparably to those from cord blood, further supporting the potential interest of leukoreduction filters. In addition, the limited quantity of RBCs destined for panels for antigen detection of rare blood groups can be produced from LDFs this way, reducing the need to solicit donors.

In order to investigate the potential of real HSPC expansion starting from steady-state blood CD34+ cells issued from LDFs, we used immunodeficient NOD/SCID mice transplanted with freshly isolated CD34+ cells maintained in ex vivo culture for 1 or 7 days. We confirmed that the engraftment capacity of these cells is low in the basal state and demonstrated that it increases after 7 days of culture. This is paralleled by an increase in the number of side population (SP) cells as well as SP+ CD34+, CD38-, CD133+ cells, a phenotypic subpopulation enriched in HSCs (11). Concerning the side population (SP) phenotype of steady-state peripheral blood cells, our second study demonstrated that they display properties of very primitive HSCs: their high proliferative capacity is dependent on low oxygen concentration, an effect dependent on both hypoxia-induced factors HIF-1 and HIF-2; they exhibit reduced mitochondrial mass as well as lower mitochondrial activity than non-SP cells (12).

Furthermore, after ex vivo expansion of the steady-state peripheral CD34+ cells, their long-term engraftment potential (hematopoietic repopulation of secondary recipient mice) was revealed, which is the first result showing the presence of LT-HSC in steady-state peripheral blood (11). These results, concerning the short-term (primary recipients) and long-term (secondary recipients) repopulating HSCs, were confirmed with immunodeficient NSG mice, which are a more appropriate model (13). In the same study, using limiting dilution analysis, we demonstrated that ex vivo culture enhances both the absolute number of repopulating HSCs and their individual proliferative capacity. Concerning immunophenotype, in vivo reconstituting cells in the steady-state blood CD34+ cell fraction before expansion are found in the CD133+ subfraction and are CXCR4 low or, to a lesser extent, CXCR4 high. After ex vivo expansion, they are found only in the CD133+CXCR4+ fraction. The failure of the CXCR4 high population to engraft is probably due to the exclusive expression of CD26 by these cells. It is obvious that these peripheral blood non-mobilized cells exhibit a different phenotype with respect to their mobilized blood, cord blood, and bone marrow counterparts.

Hematopoietic graft conception starting from steady-state peripheral blood CD34+ cells

Thus, to conceive hematopoietic grafts based on non-mobilized, steady-state hematopoietic CD34+ cells, an ex vivo passage (ex vivo expansion step) is mandatory. Our laboratory has extensive experience in the conception and development of ex vivo procedures for expansion of hematopoietic cells issued from mobilized blood (14) and cord blood (15, 16, 17) for transplantation, including the clinical trials (18, 19). However, the response to cytokines and growth factors is very

different in steady-state HSPCs with respect to their mobilized blood, bone marrow, and cord blood counterparts.

Our work consisted of optimizing the ex vivo expansion protocol of steady-state peripheral blood cells. For this purpose, we tested practically all available cytokines, growth factors, small molecules, as well as some vitamins and antioxidants. The basic cytokine cocktail (G-CSF, SCF, Tpo complemented with a low dose of IL-3) (13) can enhance the committed progenitors with a simultaneous enhancement of HSC activity. In order to potentiate these effects, we studied Interleukin-6 (IL-6; 100 ng/mL), FN (neurotrophic factors: BDNF, GDNF, NT-3, NT-4), Spermidine (10 µM and 100 µM), small molecule UM171 (35 nM), Octamer-binding transcription factor associated coactivator 1 (OAC1 (1, 2, and 10 µM), polyvinyl alcohol PVA (0.1 and 1%), low-density lipoproteins (LDL;10, 20, and 40 µg/mL), c-Jun N-terminal kinase-inhibitor 8 (JNK-IN8; 1 µM), and alpha-lipoic acid (ALA; 100 µM). The effects were dependent on the medium used for expansion: for example, ALA showed a positive impact in Stem Span™ SFEM II supplemented with 100 ng/mL rhSCF (Peprotech, Neuilly-sur-Seine, France), 100 ng/mL rhFlt-3L (Peprotech), 20 ng/mL rhTPO (Peprotech), and 10 ng/mL rhG-CSF (Neupogen; AMGEN, Boulogne Billancourt, France). In these conditions, ALA increased the ex vivo expansion of total CD34+ cells and of phenotypically defined CD34+ HSPC subpopulations that retained in vivo repopulating capacity, concomitantly with a decreased expansion of differentiating cells (20).

However, in clinical-grade culture setups, the combination of StemRegenin 1 (SR1) and the small molecule (UM729) revealed to be most promising (work in progress).

Conclusion

With respect to the source of steady-state peripheral blood HSPCs for a hematopoietic graft, it is possible to consider either cytaphereses performed without prior mobilization (one to three procedures plus ex vivo expansion are estimated to be sufficient to obtain the critical number of CD34+ cells) or LDF-derived cells cryopreserved after several blood donations.

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ASSESSMENT OF IRON STATUS IN REGULAR PLATELETPHERESIS DONORS: A CROSS-SECTIONAL STUDY

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Abstract

Regular plateletpheresis donors represent a specific population of voluntary blood donors in whom frequent donation procedures may lead to gradual depletion of iron stores despite normal hemoglobin values. The aim of this study was to evaluate iron status in regular plateletpheresis donors and compare the findings with first-time blood and platelet donors. The study included donors who underwent plateletpheresis procedures at the Blood Transfusion Institute of Vojvodina during the previous two years. Complete blood count parameters and iron metabolism indicators, including hemoglobin, hematocrit, erythrocyte indices, serum iron, and ferritin, were analyzed. In regular donors, mean hemoglobin values and erythrocyte indices remained within reference ranges, while ferritin and serum iron levels were lower compared with first-time donors. Ferritin levels below 50 ng/mL were detected in 16% of participants, while nearly half of the donors had ferritin values below 100 ng/mL. The obtained results indicate that normal hemoglobin values do not exclude latent iron deficiency in frequent platelet donors. Periodic ferritin testing may contribute to early detection of depleted iron stores and improvement of donor safety.

Key words: plateletpheresis; ferritin; blood donors

Sažetak

Zbog učestalosti afereznih procedura, redovni davaoci trombocita mogu biti izloženi povećanom riziku od razvoja latentnog deficita gvožđa, koji se često ne manifestuje sniženjem koncentracije hemoglobina. Cilj ovog rada bio je da se proceni status gvožđa kod redovnih davalaca trombocita postupkom trombocitafereze i da se rezultati uporede sa kontrolnom grupom koju su činili novi davaoci koji nikad nisu donirali celu krv ili trombocite. Studija je obuhvatila davaoce koji su tokom prethodne dve godine davali trombocite u Zavodu za transfuziju krvi Vojvodine. Analizirani su parametri kompletne krvne slike i metabolizma gvožđa, uključujući hemoglobin, hematokrit, eritrocitne indekse, serumsko gvožđe i feritin. Kod redovnih davalaca prosečne vrednosti hemoglobina i eritrocitnih indeksa bile su u referentnim granicama, dok su vrednosti feritina i serumskog gvožđa bile niže u odnosu na kontrolnu grupu. Feritin niži od 50 ng/mL registrovan je kod 16% ispitanika, dok je skoro polovina davalaca imala vrednosti feritina niže od 100 ng/mL. Dobijeni rezultati ukazuju da referentne vrednosti hemoglobina ne isključuju prisustvo latentne sideropenije kod učestalih davalaca trombocita. Periodično određivanje feritina može doprineti ranom otkrivanju smanjenih rezervi gvožđa i unapređenju bezbednosti davalaca krvi.

Ključne reči: trombocitafereza; feritin; davaoci krvi

Introduction

Plateletpheresis represents one of the most important procedures in modern transfusion medicine, considering the continuous increase in demand for platelet concentrates used in the treatment of hematological, oncological, and surgical patients. Platelet concentrates obtained by apheresis enable collection of a therapeutic platelet dose from a single donor, thereby reducing recipient exposure to multiple donors and decreasing the risk of transfusion reactions and alloimmunization (1).

Due to the growing demand for platelet concentrates, the number of voluntary donors participating in repeated plateletpheresis procedures has also increased. Although most erythrocytes are returned to the donor during the procedure, repeated apheresis donations may lead to cumulative iron loss (2, 3). During each procedure, a certain amount of red blood cells remains in the cell separators and tubing systems, which over time may result in gradual depletion of iron stores and development of latent iron deficiency (4).

Traditional blood donor screening is primarily based on hemoglobin determination. Hemoglobin is the main parameter used for donor eligibility assessment in most transfusion centers worldwide (4). However, numerous studies have shown that hemoglobin values may remain within the reference range despite significantly reduced iron stores (2-5). Iron deficiency initially manifests as depletion of iron reserves and reduced ferritin concentration, while hemoglobin decline occurs only in later stages of iron deficiency development (6).

Ferritin is considered the most important marker of body iron stores and a more sensitive indicator of latent iron deficiency than hemoglobin alone. Contemporary studies have demonstrated that a large proportion of regular platelet donors may have normal complete blood count findings despite reduced ferritin levels. Consequently, an increasing number of transfusion centers have introduced periodic ferritin testing as part of donor safety monitoring programs (7).

In addition to iron depletion, long-term and frequent plateletpheresis may also affect other hematological parameters. Several studies have reported gradual decreases in hematocrit, red blood cell count, and serum iron levels in donors with a high annual number of apheresis procedures (7–9). Nevertheless, results among studies remain inconsistent, likely due to differences in donor populations, donation frequency, sex distribution, and criteria used to define iron deficiency.

Preservation of voluntary donor health is one of the fundamental principles of transfusion medicine. Regular donors represent a crucial component of the blood supply system, and their long-term health status is of great importance. In recent years, increasing attention has been focused on developing iron status monitoring programs for regular blood donors, particularly plateletpheresis donors who are at increased risk of latent iron deficiency (1, 6).

Considering the importance of preserving donor health, as well as the limitations of routine hemoglobin determination in assessing iron status, the aim of this study was to evaluate iron status in regular plateletpheresis donors through analysis of complete blood count parameters, serum iron, and ferritin levels, and to compare the findings with those obtained in first-time blood and platelet donors without previous donation history.

Materials and methods

The study included plateletpheresis donors who donated platelets by donor plateletpheresis procedures at the Blood Transfusion Institute of Vojvodina during the previous two years. Complete blood count parameters and iron metabolism indicators were analyzed, including hemoglobin, hematocrit, erythrocyte indices, serum iron, and ferritin.

The control group consisted of donors who donated blood or platelets for the first time and had no previous donation history. Laboratory parameters obtained through routine biochemical and hematological analyses were evaluated in all participants.

The results were presented using descriptive statistical methods. Continuous variables were expressed as mean values and standard deviations, while categorical variables were presented as percentages. The obtained results were compared between regular and first-time donor groups.

Results

In the group of regular plateletpheresis donors, complete blood count and iron metabolism parameters were analyzed over a two-year period. The median annual number of donations was 23.5, ranging from 15 to 48 procedures, indicating that most participants belonged to the group of frequent platelet donors.

Analysis of hematological parameters demonstrated that mean hemoglobin values and erythrocyte indices were generally within reference ranges. Mean hemoglobin concentration was 153.0 ± 8.5 g/L, while the average hematocrit value was 0.46 ± 0.03 L/L. The mean erythrocyte count was 5.06 ± 0.33 $\times 10^{12}$/L. Erythrocyte indices also showed no significant abnormalities: mean MCV was 90.8 ± 4.4 fL and mean MCH was 30.4 ± 1.5 pg. These findings indicate that manifest anemia and significant erythrocyte morphological changes were not present in the majority of regular donors.

However, analysis of iron metabolism parameters demonstrated considerably different results. Mean ferritin concentration was 104.2 ± 50.8 ng/mL, with a median value of 102.5 ng/mL and a range from 23 to 263 ng/mL. Although average ferritin values were within reference limits, detailed analysis revealed latent iron deficiency in a substantial proportion of donors.

Ferritin values below 30 ng/mL were detected in 2 donors (4%), while ferritin levels below 50 ng/mL were found in 8 donors (16%). Particularly significant was the finding that nearly half of the participants, 24 out of 50 donors (48%), had ferritin levels below 100 ng/mL, which may indicate gradual depletion of iron stores associated with frequent plateletpheresis procedures.

Compared with the control group of first-time blood and platelet donors, regular plateletpheresis donors demonstrated lower iron metabolism parameters. Mean ferritin concentration in regular donors was 104.2 ± 50.8 ng/mL, whereas in first-time donors it was 145.2 ± 98.9 ng/mL (p=0.015). In addition, mean serum iron levels were lower in regular donors compared with controls (20.5 ± 8.0 vs. 24.8 ± 8.4 μmol/L; p=0.014).

On the other hand, hemoglobin values did not differ significantly between groups. Mean hemoglobin concentration in regular donors was 153.0 ± 8.5 g/L, compared with 150.6 ± 9.1 g/L in first-time donors (p=0.20). These findings indicate

that normal hemoglobin values do not exclude reduced iron stores in frequent platelet donors.

The obtained findings are consistent with contemporary studies demonstrating that regular plateletpheresis procedures may lead to latent iron deficiency even in donors with normal hematological parameters. Particularly important is the observation that changes are first detected through decreased ferritin and serum iron levels, while hemoglobin often remains within reference ranges.

Discussion

Preservation of voluntary donor health represents one of the primary goals of transfusion medicine. In recent years, increasing numbers of studies have emphasized the importance of monitoring iron stores in regular blood donors, particularly plateletpheresis donors.

The results of this study demonstrate that hemoglobin alone is not a sufficient indicator of iron status. Reduced ferritin levels were identified even in donors with normal complete blood count findings. Similar findings have been reported in numerous studies emphasizing the need for routine ferritin determination in frequent platelet donors (7–10).

Development of latent iron deficiency in plateletpheresis donors may have important health consequences, including fatigue, decreased exercise tolerance, and reduced quality of life. Although symptoms often do not develop immediately, prolonged depletion of iron stores may eventually lead to overt iron deficiency anemia (2, 7).

Several studies have identified donation frequency as one of the most important risk factors for iron depletion. Spencer et al. demonstrated that the risk significantly increases in donors with a higher annual number of plateletpheresis procedures, even in the presence of normal hemoglobin levels (7). Similar findings were reported by Odajima et al. in a study conducted among Japanese plateletpheresis donors, where a significant proportion of donors had reduced ferritin levels despite normal hemoglobin values (8).

Current recommendations increasingly emphasize an individualized approach to donor monitoring (8–11). In addition to hemoglobin testing, periodic assessment of iron stores, particularly ferritin determination, is recommended for frequent platelet donors. The findings of the present study confirm that hemoglobin alone is insufficient for assessing iron status, as reduced ferritin levels may occur despite normal hematological parameters. Ferritin is a more sensitive indicator of iron reserves and enables early detection of latent iron deficiency. Routine ferritin monitoring may facilitate timely preventive measures, including extension of donation intervals or iron supplementation, thereby improving long-term donor safety and supporting the sustainability of voluntary blood donation programs.

Conclusion

Regular plateletpheresis donors may have preserved hemoglobin values despite reduced iron stores. Ferritin represents a more sensitive marker of iron deficiency than hemoglobin and may play an important role in donor monitoring. Periodic ferritin testing in frequent platelet donors may facilitate early detection of iron depletion and support evidence-based donor management.

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AUTOMATED DONOR ERYTHROCYTAPHERESIS AS A TOOL FOR RATIONAL BLOOD INVENTORY MANAGEMENT – EXPERIENCE OF THE BLOOD TRANSFUSION INSTITUTE OF VOJVODINA

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Abstract

Automated donor erythrocytapheresis is a modern transfusion procedure that enables targeted collection of two units of red blood cells from a single donor during one donation while simultaneously returning other blood components to the donor. The implementation of this procedure contributes to more rational blood inventory management, increases the efficiency of red blood cell collection, and enables the production of high-quality and standardized blood components. The particular importance of the procedure lies in reducing patient exposure to multiple donors, which is especially important in hematological and oncological patients requiring long-term transfusion therapy. This report presents the experience of the Blood Transfusion Institute of Vojvodina in the implementation of automated donor erythrocytapheresis during the period from August 9, 2022 to May 1, 2026. During the observed period, a total of 567 procedures were performed, providing approximately 1134 red blood cell units. The majority of donors were repeat voluntary blood donors, predominantly male. Quality control analysis demonstrated a high degree of product standardization, minimal residual leukocyte count, and confirmed microbiological safety. No severe donor adverse reactions were recorded. The obtained results confirm that automated donor erythrocytapheresis is a safe and efficient procedure with an important role in modern and rational blood inventory management.

Key words: erythrocytapheresis; red blood cell components; blood donors

Sažetak

Automatizovana donorska eritrocitafereza predstavlja savremenu transfuzijsku proceduru kojom se tokom jedne donacije selektivno prikupljaju dve terapijske jedinice eritrocita od jednog davaoca, uz istovremeno vraćanje preostalih krvnih komponenti u cirkulaciju davaoca. Primena ove procedure doprinosi racionalnijem upravljanju zalihama krvi, povećava efikasnost prikupljanja eritrocita i omogućava dobijanje visokokvalitetnih i standardizovanih krvnih komponenti. Automatizovana eritrocitafereza ima poseban značaj u transfuzijskom lečenju jer omogućava smanjenje broja ekspozicija primaoca alogenim davaocima. Ovakav pristup može doprineti smanjenju rizika od eritrocitne aloimunizacije i drugih imunološki posredovanih neželjenih reakcija povezanih sa transfuzijom, posebno kod pacijenata na programu hronične transfuzijske terapije. U radu su prikazana iskustva Zavoda za transfuziju krvi Vojvodine u primeni automatizovane donorske eritrocitafereze u periodu od 9. avgusta 2022. do 1. maja 2026. godine. Tokom posmatranog perioda izvedeno je ukupno 567 procedura, čime je obezbeđeno približno 1134 jedinice eritrocita. Većinu davalaca činili su višestruki dobrovoljni davaoci krvi, dominantno muškarci. Analiza kvaliteta komponenti pokazala je visok stepen standardizacije produkata, minimalan broj rezidualnih leukocita i potvrđenu mikrobiološku bezbednost. Nisu zabeležene ozbiljne neželjene reakcije kod davalaca. Dobijeni rezultati potvrđuju da automatizovana donorska eritrocitafereza predstavlja bezbednu i efikasnu proceduru sa značajnom ulogom u savremenom i racionalnom upravljanju zalihama krvi.

Ključne reči: eritrocitafereza; eritrocitne komponente; davaoci krvi

Introduction

Modern transfusion medicine faces continuous challenges in ensuring sufficient quantities of safe and high-quality blood components. Increased demands from clinical centers, the growing number of complex surgical procedures, advances in hematological and oncological therapies, and prolonged life expectancy have all contributed to a continuous rise in the consumption of red blood cell components. At the same time, transfusion institutions worldwide face difficulties in recruiting and retaining voluntary blood donors, making rational management of existing blood resources one of the major priorities of contemporary transfusion medicine (1).

Automated donor erythrocytapheresis (ADE) represents one of the most important modern technologies in the field of apheresis blood component collection. The procedure enables selective collection of red blood cells using automated cell separators while returning plasma and other blood components to the donor. Unlike standard whole blood donation, a single ADE procedure allows the collection of two therapeutic units of red blood cells from one donor, significantly increasing the efficiency of red blood cell collection (2).

The particular importance of erythrocytapheresis lies in reducing recipient exposure to multiple donors. This aspect is especially important in hematological and oncological patients, as well as in patients with chronic anemia who require long-term transfusion therapy. Administration of red blood cell components from a single donor may contribute to reducing the risk of alloimmunization, febrile non-hemolytic transfusion reactions, and other immunological complications of transfusion therapy (2–4).

An additional advantage of automated apheresis procedures is the high degree of blood component quality standardization. Modern cell separators allow precise control of product volume, hematocrit, hemoglobin content, and leukodepletion level (5). This ensures a uniform product quality that complies with Council of Europe and EDQM standards (2).

At the Blood Transfusion Institute of Vojvodina, the ADE program was introduced with the aim of improving red blood cell inventory management, particularly for patients requiring multiple transfusions or red blood cells with specific blood group characteristics. In addition to increasing the efficiency of red blood cell collection, special emphasis was placed on donor safety, appropriate donor selection, and quality control of final blood products.

The aim of this study was to present the experience of the Blood Transfusion Institute of Vojvodina in the implementation of automated donor erythrocytapheresis through the analysis of procedure numbers, donor characteristics, and the quality of collected red blood cell components in the period from August 2022 to May 2026.

Materials and methods

This retrospective study included all automated donor erythrocytapheresis procedures performed at the Blood Transfusion Institute of Vojvodina between August 9, 2022 and May 1, 2026.

The study included voluntary blood donors who met the criteria for apheresis procedures according to current national recommendations. Inclusion criteria included adequate hemoglobin and hematocrit values, body weight above 70 kg, appropriate estimated blood volume, and absence of contraindications for apheresis procedures.

ADE procedures were performed using automated cell separators with sterile disposable sets and citrate anticoagulant. During each procedure, two units of red blood cells were collected with simultaneous volume replacement using saline solution. The duration of the procedure was approximately 30–40 minutes.

Demographic donor data, number of procedures performed, donation frequency, and ABO blood group distribution were analyzed. The quality of apheresis red blood cell components was assessed by determining product volume, hematocrit, hemoglobin content, residual leukocyte count, and sterility of components.

Results were presented using descriptive statistical methods as mean value ± standard deviation and range.

Results

During the period from August 9, 2022 to May 1, 2026, a total of 567 automated donor erythrocytapheresis procedures were performed at the Blood Transfusion Institute of Vojvodina.

Analysis of donor structure showed that the program was predominantly based on previously registered regular voluntary blood donors. Of the total procedures performed, 541 were carried out in repeat donors, while 26 procedures involved first-time donors. This structure highlights the importance of continuous monitoring and retention of carefully selected donors suitable for apheresis procedures.

The vast majority of procedures (565/567) were performed in male donors, while only two procedures were performed in female donors. This distribution was expected given the eligibility requirements for automated donor erythrocytapheresis, including higher body weight, hemoglobin concentration, and estimated circulating blood volume.

Regarding donation frequency, 241 donors underwent a single erythrocytapheresis procedure during the study period, while many donors participated in the program on multiple occasions. One donor particularly stood out with a total of ten successfully completed erythrocytapheresis procedures, confirming the possibility of long-term sustainability of the program in carefully selected and adequately monitored donors. Considering that two red blood cell units were collected during each procedure, approximately 1134 red blood cell units were obtained through the ADE program during the observed period, significantly contributing to the maintenance of red blood cell inventories and transfusion support for patients requiring chronic or urgent transfusion therapy.

Analysis of ABO blood group distribution showed the highest prevalence of blood group O donors (268), followed by blood groups A (233), B (53), and AB (13). The high prevalence of blood group O donors is of particular importance for the transfusion system due to the frequent need for these red blood cell components in emergency and urgent transfusion settings.

Quality control of apheresis red blood cell components demonstrated a high degree of product standardization and compliance with EDQM quality standards. The mean unit volume was 250 ± 3 mL, ranging from 245 to 255 mL. Mean hematocrit value was 59.7 ± 4.1%, while mean hemoglobin content was 54.5 ± 6 g per unit.

A particularly important finding was the low residual leukocyte count. The mean value was 0.05 ± 0.02 $\times 10^6$/unit, indicating a high degree of leukodepletion and efficiency of the automated component preparation system. Reduced leukocyte content is of particular clinical importance in patients requiring multiple transfusions, as it contributes to reducing the risk of febrile non-hemolytic transfusion reactions, HLA alloimmunization, and other immunomodulatory effects of transfusion.

Sterility of all analyzed components was 100%, confirming the safety of the procedure and adequate quality control of blood component preparation.

No severe donor adverse reactions requiring interruption of the procedure or additional medical intervention were recorded during the observed period, confirming the high safety profile and good donor tolerance of automated donor erythrocytapheresis.

Discussion

Automated donor erythrocytapheresis currently represents one of the most important developments in modern transfusion medicine, particularly in the context of rational blood resource management and improvement of transfusion therapy quality. Compared with standard whole blood donation, automated donor erythrocytapheresis enables collection of approximately double the amount of red blood cells during a single donation session, thereby significantly improving the efficiency of blood collection and inventory management. This approach is particularly important during periods of reduced blood supply, increased clinical demand, and for the collection of units from donors with rare or highly required blood group phenotypes (6).

The predominance of repeat donors suggests good tolerability of the procedure and successful retention of motivated donors within the apheresis program. Similar experiences have been reported by other transfusion institutions, emphasizing that apheresis donation programs are usually based on a group of regular, highly motivated donors with long-standing voluntary blood donation experience (7, 8).

The predominance of male donors was expected considering the erythrocytapheresis selection criteria, which include higher body weight, higher hemoglobin and hematocrit values, and adequate estimated circulating blood volume. Similar findings were reported by Pehlic et al., who stated that men constitute the dominant donor population included in double red blood cell apheresis programs due to physiological and hematological characteristics that enable safe performance of the procedure (9).

One of the most important findings of this study is the high degree of standardization of apheresis red blood cell quality. Uniform values of volume, hematocrit, and hemoglobin content confirm the precision of modern automated separators and the high level of quality control during component preparation. Similar results were published by Simon et al., who emphasized that automated systems provide significantly greater standardization of red blood cell components compared to components derived from whole blood donations (10). Standardized product quality is particularly important in daily clinical practice because it enables a more predictable therapeutic transfusion effect and more precise transfusion therapy planning.

A particularly important aspect of automated erythrocytapheresis is the very low residual leukocyte content. Modern automated systems achieve a high degree of leukodepletion during the procedure itself, reducing the need for additional component processing. Leukodepletion has major clinical significance because it reduces the risk of febrile non-hemolytic transfusion reactions, HLA alloimmunization, transmission of leukocyte-associated cytokines, and immunomodulatory transfusion effects. Numerous studies have shown that leukodepletion significantly contributes to reducing adverse transfusion reactions in chronically transfused patients, particularly in hematological and oncological patients (10–12).

In patients who are chronically transfusion-dependent, one of the major problems is the development of alloimmunization against erythrocyte antigens, which may significantly complicate future transfusion therapy and the identification of compatible blood components. Therefore, a major advantage of ADE lies in reducing patient exposure to multiple donors. Vamvakas and Blajchman reported that reducing exposure to different donors may significantly decrease immunological complications associated with transfusion therapy. This aspect is particularly important in hematological and oncological patients receiving large numbers of red blood cell transfusions during treatment (12).

In addition to its clinical significance for recipients, automated erythrocytapheresis also plays an important organizational role in transfusion institutions. The possibility of targeted production of red blood cell components is particularly important for donors with rare blood groups, phenotype-specific donors, and during periods of increased blood demand. The predominance of blood group O donors in this study additionally emphasizes the strategic importance of ADE in maintaining adequate inventories of universally applicable red blood cell components, particularly in emergency and intensive care settings. According to data from European transfusion centers, O RhD negative red blood cells represent one of the most deficient blood components in everyday clinical practice, making apheresis collection of these components strategi-

cally important (7, 9, 10). Modern cell separators enable a high degree of process automation and significantly reduce the possibility of errors during component preparation. At the same time, reinfusion of plasma and other blood components contributes to better hemodynamic tolerance of the procedure and faster recovery compared to standard whole blood donation. However, several authors have pointed out that frequent erythrocytapheresis procedures may gradually reduce iron stores in donors. Cable et al., as well as Kiss and Vassallo, emphasized the importance of continuous monitoring of hematological parameters and iron status in donors participating in intensive apheresis donation programs, especially repeat erythrocytapheresis donors (8, 9). Although ADE offers numerous clinical and organizational advantages, continuous monitoring of hemoglobin values and iron stores in repeat donors remains essential for preservation of donor safety and long-term sustainability of the program. Several authors emphasize that regular assessment of iron metabolism parameters and individualized donor follow-up may contribute to prevention of latent iron deficiency in frequent erythrocytapheresis donors (10-13).

Overall, the present findings support the role of automated donor erythrocytapheresis as an effective strategy for the production of high-quality red blood cell components and for optimizing blood inventory management.

Conclusion

The experience of the Blood Transfusion Institute of Vojvodina confirms that automated donor erythrocytapheresis is a safe and effective method for the collection of high-quality, standardized red blood cell components. In addition to improving the availability of red blood cell units, this procedure contributes to rational blood inventory management and reduces recipient exposure to multiple allogeneic donors. Automated donor erythrocytapheresis therefore represents an important component of contemporary transfusion practice and sustainable blood component management.

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THE SIGNIFICANCE AND ROLE OF THE TRANSFUSIOLOGIST IN TISSUE AND ORGAN TRANSPLANTATION

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Abstract

Transfusiology, or transfusion medicine, is a multidisciplinary science whose primary role and significance lie in the management of patients requiring blood therapy. In addition to this fundamental role, it also has great importance in tissue and organ transplantation. As a science, it may be regarded as a relatively young, specialized branch of medicine, a discipline that experienced its greatest expansion during the twentieth century. The development and expansion of tissue and organ transplantation over the past two decades have also contributed to the development of clinical transfusiology and to its role in transplantation. The increasingly broad indications for tissue and organ transplantation in modern medicine have involved transfusiologists in the technology of collecting, preserving, and storing tissues and organs, particularly hematopoietic stem cells from bone marrow, peripheral blood, and umbilical cord blood. Transfusiologists have found their place and play a role throughout the entire pre-transplantation, transplantation, and post-transplantation period of patients currently treated by tissue and organ transplantation. In addition to providing blood support to patients before, during, and after transplantation, the testing of blood groups in both tissue and organ recipients and donors is of major importance. A special role of the transfusiologist is the determination of tissue compatibility through HLA typing and the selection of the most compatible donor. The preparation and administration of compatible blood and blood components are particularly important during this period in order to avoid adverse immunological reactions in the post-transplantation period.

Keywords: transfusiologist, tissue and organ transplantation, tissue compatibility, blood transfusion

Sažetak

Transfuziologija ili transfuzijska medicina predstavlja multidisciplinarnu nauku, čija je osnovna uloga i značaj u zbrinjavanju bolesnika sa krvlju. Pored ove osnovne uloge ona ima veliki značaj i u transplantaciji tkiva i organa. Kao nauka, može se posmatrati kao mlađa, specijalizovana grana medicine, disciplina koja je najveću ekspanziju doživela tokom XX veka. Transplantacija tkiva i organa i njena ekspanzija u poslednje dve decenije doprinela je i razvoju kliničke transfuziologije i njenom doprinosu u transplantaciji. Sve šire indikacije za transplantaciju tkiva i organa u savremenoj medicini uključile su i transfuziologe u tehnologiji prikupljanja, konzervisanja i čuvanja tkiva i organa, a naročito matične ćelije hematopoeze (MĆH) iz kostne srži, periferne i umbilikalne krvi. Transfuziolozi su našli mesto i imaju ulogu u kompletnom pretransplantacionom, transplantacionom i posttransplantacionom periodu pacijenata koji se danas leče transplantacijom tkiva i organa. Pored zbrinjavanja pacijenata sa krvlju u periodu pre, u toku i posle transplantacije veliki značaj ima i ispitivanje krvnih grupa primaoca tkiva i organa a takođe i davaoca tkiva i organa. Posebna uloga transfuziologa je u određivanju podudarnosti tkiva HLA tipizacija i odabiru najpodudarnijeg donora.Priprema i primena kompatibilne krvi i komponenata krvi naročito je značajna u ovom periodu, a u cilju izbegavanja neželjenih imunoloških reakcija u postransplantacionom periodu.

Ključne reči: transfuziolog, transplantacija tkiva i organa, tkivna podudarnost, transfuzija krvi

Introduction

Tissue and organ transplantation is a complex branch of modern medicine, recognizing solid-organ and tissue transplantation as one of the most complex and humane treatment methods for patients with terminal failure of vital organs. The success of this procedure goes beyond the boundaries of a single medical specialty and relies on the highly coordinated work of a multidisciplinary team. Within this team, the transfusion medicine specialist occupies a critical, highly specialized, central, and irreplaceable position. The transfusiologist primarily ensures the immunological safety of the entire process,

manages specific blood components, and directly contributes to reducing the risk of graft rejection (1, 2).

Clinical transfusion medicine includes the therapeutic use of blood, various forms of transplantation and histocompatibility, numerous methods that support transfusion and transplantation, associated disciplines, the management of blood donor registries, bone marrow and stem-cell donor registries, patient registries, the establishment of national biobanks, centralized prenatal care, the development of information technologies, and many other areas imposed by modern medicine. Contemporary knowledge in human genetics and molecular biology has enabled analysis of the genetics of blood-group antigens and the HLA system (3).

Historical Development of Transplantation Medicine

Historically, after it became known that hematopoietic stem cells committed to individual lineages originate from a single pluripotent stem cell, research began into the possibility of using bone marrow transplantation in the treatment of malignant hematological diseases, with the first results appearing in the middle of the last century. A large proportion of these transplantations were unsuccessful because they were based on a syngeneic transplantation model and did not take into account the existence and importance of compatibility within the histocompatibility system. Further research led to progress in understanding the importance of the HLA system and later, in the post-transplantation period, to solving the problem of graft-versus-host disease (GvHD).

The idea of replacing diseased parts of the body is much older. Physicians also worked on this issue in more recent history, but there were many medical and technical challenges. The development of organ transplantation was made possible by animal experiments, especially in mice. Between 1900 and 1930, the first cadaveric kidney transplantation was performed in one patient, but it ended unsuccessfully. The first successful human kidney transplantation was performed in Boston in 1954, and since then, thanks to the use of immunosuppressive therapy, patient survival has improved.

The role of the transfusiologist has evolved over history from that of a specialist who provides and tests whole blood to that of a clinical consultant involved in genetic selection, immunological monitoring, and perioperative hemostatic management. Without advances in transfusion medicine and immunogenetics, most modern organ transplantation procedures would fail because of insurmountable immunological barriers (1, 4).

Transplantation Medicine

Tissue or organ transplantation and blood transfusion are closely connected. Since its introduction, blood transfusion has been, and remains, the first form of tissue transplantation in patients, although it is not approached as transplantation of another tissue or organ but rather as replacement of blood and blood components. However, because it can also produce adverse reactions, it should be considered a transplantation of blood. The use of blood transfusion is a serious therapeutic method and a very complex challenge for the immune system of every patient. In organ transplantation and the use of blood transfusion, one could speak of a dual transplantation, because in addition to organ transplantation, transplantation of a liquid tissue—blood—is also performed (1, 5).

The introduction of foreign cells, such as erythrocytes, platelets, and leukocytes, into the recipient's body triggers a whole series of immunological cascades that directly affect the survival and acceptance of solid organs and tissues (6). The transfusiologist must have a strong knowledge of cellular immunology, genetics, the pathophysiology of hemostasis, and advanced laboratory technologies. Their role extends through three key phases: preoperative evaluation, intraoperative support, and postoperative monitoring.

Tissue or organ transplantation is very often the only effective treatment option for patients with irreversible tissue or organ damage and frequently with potentially fatal outcomes. The number of tissue and organ transplantations worldwide is increasing every day, and transplantation is considered one of the most advanced treatment methods. Bone marrow transplantation is the method of choice in hematological diseases when other therapies do not produce results.

An integral part of tissue and organ transplantation is transfusion support, meaning the replacement of blood, blood components, and blood products. Therefore, transfusiologists, as members of the transplantation team, are responsible for ensuring safe blood, diagnosing disorders of blood hemostasis, preventing transmissible diseases, and minimizing the frequency of potential immunomodulatory effects associated with the use of allogeneic and autologous blood. The role of the transfusiologist in the treatment of a patient for whom transplantation has been selected as the treatment method can be divided into the pre-transplantation or preoperative phase, the transplantation or operative phase, and the post-transplantation or postoperative phase (1, 7).

1. Pre-transplantation Period or Preoperative Phase

In the pre-transplantation period, pre-transfusion investigations must be performed, including determination of ABO and RH blood groups and other blood-group systems for both recipient and donor, HLA typing of the recipient and potential donor, screening for preformed anti-HLA antibodies, cross match tests, and markers of transmissible diseases.

ABO-incompatible organ transplantation was considered an insurmountable obstacle in solid-organ transplantation for many years. Organ shortage forced the medical community to develop ABO-incompatible protocols, primarily in liv-

ing-donor kidney and liver transplantation. The transfusiologist performs isohemagglutinin titration, desensitization, and safety evaluation by monitoring titer levels. Postoperative titer monitoring is carried out during the first two weeks after surgery.

The basic prerequisite for successful transplantation of an allogeneic organ or tissue is overcoming the recipient's immunological barrier. The immune system has a natural ability to distinguish self-antigens from foreign molecules. The main antigen system that mediates this process is the major histocompatibility complex (MHC), known in humans as human leukocyte antigens (HLA). HLA genes are located on the short arm of chromosome 6 and are characterized by a high degree of polymorphism. In the tissue compatibility laboratory, the transfusiologist performs typing of class I HLA loci (HLA-A, HLA-B, HLA-C) and class II loci (HLA-DR, HLA-DQ, HLA-DP). Serological methods, such as microcytotoxicity tests, were formerly used for this purpose, while molecular PCR techniques are used today (1).

A particular challenge in the preoperative phase is posed by patients who are already sensitized to foreign HLA antigens. Allosensitization occurs as a consequence of previous blood transfusions, pregnancies, and previous failed transplantations. These patients have preformed anti-HLA antibodies in circulation. If such a patient receives an organ whose cells express an antigen against which the recipient already has antibodies, hyper acute rejection occurs.

If antibodies against a donor HLA antigen are present in the recipient, hyperacute graft rejection occurs in approximately 80% of such transplantations. Despite strong immunosuppressive therapy, HLA compatibility between donor and recipient remains one of the most important conditions for a favorable transplantation outcome, particularly in bone marrow transplantation. Around 30% of patients have an HLA-identical related donor, while registries of unrelated stem-cell donors include approximately 30 million people.

Immunization by blood transfusions is common and proportional to the number of transfusions received, as well as to the frequency of HLA antigens in the population. Around 50% of individuals never produce cytotoxic anti-HLA antibodies, which may be explained by cross-reactivity of HLA antigens, the formation of blocking antibodies that bind complement, or the requirement for a specific allele in order to generate an immune response to each HLA determinant. Cytotoxic anti-HLA antibodies cause non-hemolytic febrile transfusion reactions, which may occur between 30 minutes and 2 hours after the start of transfusion. The severity of the reaction depends on the number of leukocytes transfused (1).

A frequent route of HLA antigen exposure is through transfusions of blood, platelets, or leukocytes. Platelets and leukocytes carry a large number of HLA molecules on their membranes, even more than many other tissues. With frequent transfusions, especially platelet and leukocyte transfusions, the recipient is exposed to numerous foreign HLA antigens, resulting in the formation of multiple specific anti-HLA antibodies. During repeated transfusions, these antibodies destroy transfused donor cells, especially leukocytes and platelets. Therefore, the formation of HLA antibodies should be prevented in advance and post-transfusion non-hemolytic reactions avoided. This is achieved by selecting the most HLA-compatible donor from among family members or from a panel of typed donors, and by using blood transfusions with reduced numbers of leukocytes and platelets.

If the patient's condition requires the use of blood and blood components and transplantation is planned, it is necessary to prepare blood and components that will minimize patient sensitization. Very often, when stem-cell transplantation is performed, transfusiologists carry out the collection or separation of donor stem cells that will be transplanted into the recipient or cryopreserved for planned transplantation (7).

Crossmatch tests are performed immediately before the surgical procedure itself, and their purpose is to directly expose the recipient's serum to donor lymphocytes. The transfusiologist analyzes and synthesizes the results, enabling faster decision-making in organ allocation and saving valuable organ ischemia time. The transfusiologist also performs regular screening of the serum of patients on waiting lists.

2. Transplantation Period or Operative Phase

Transfusiologists prepare blood and blood components, with prior preparation of the donor for supportive therapy that is necessary in the period after transplantation. Blood components administered to patients during transplantation must not be prepared in the standard way. The transfusiologist performs triage and indicates special technological processes for blood processing. All blood components, including erythrocyte and platelet concentrates intended for transplant patients, must undergo leukodepletion, meaning removal of white blood cells using highly efficient filters so that fewer than 1×10^6 leukocytes remain per unit. The reasons for this include prevention of HLA allosensitisation, reduction of cytomegalovirus transmission, and irradiation of blood components (1, 7, 8).

Modern transfusion medicine standards require the use of viscoelastic methods directly at the patient's bedside through point-of-care devices for rotational thromboelastometry (ROTEM) and thromboelastography (TEG). The transfusiologist interprets the ROTEM curve in real time, within 5–10 minutes, and applies targeted massive transfusion protocols. This substantially reduces unnecessary exposure of the patient to allogeneic blood components and lowers the risk of transfusion-associated circulatory overload and transfusion-related acute lung injury (2).

3. Post-transplantation Period or Postoperative Phase

After the transplantation period, the transfusiologist remains involved in long-term patient monitoring through the detection and treatment of immunological complications, control of the possible presence of HLA antibodies, and possible development of antibodies against other blood-group systems that were examined in the pre-transplantation period. The role of the transfusiologist in this period is important because of the preparation of supportive therapy and the provision of donors for platelet concentrate support (9–11).

In the event of acute antibody-mediated rejection, although the patient is receiving immunosuppressive therapy, the immune system may subsequently develop specific antibodies against the donor, known as de novo donor-specific antibodies. The appearance of these antibodies directly indicates the development of acute or chronic antibody-mediated organ rejection. In cooperation with clinicians, the transfusiologist performs therapeutic plasma exchange, or plasmapheresis (12–14).

The Role of the Transfusiologist in Tissue Transplantation and Tissue Banking

Transplantation of human tissues, such as bone, tendons, skin, corneas, heart valves, and amniotic membrane, is a standard branch of modern regenerative medicine. The organization, management, quality control, and safety of tissue and cell banks are directly entrusted to specialists in transfusion medicine. In tissue banking, the transfusiologist applies the principles of good manufacturing practice and rigorous legal regulations, including donor evaluation, stringent testing, processing, cryopreservation, and sterilization (3, 15). The transfusiologist performs detailed screening of donor medical history and social behavior, whether from living or cadaveric donors, in order to eliminate risk factors. Every tissue donor must undergo rigorous serological and molecular testing, including nucleic acid testing, for blood-borne pathogens such as HIV types 1 and 2, hepatitis B, hepatitis C, and syphilis. The transfusiologist supervises tissue processing under sterile conditions, including clean rooms, the use of antibiotics, or gamma sterilization of grafts. They also implement and manage long-term tissue storage processes. Cellular grafts and certain tissues, such as heart valves and stem cells, require freezing at controlled cooling rates with the addition of cryoprotective agents such as dimethylsulfoxide and storage at liquid nitrogen temperatures. The transfusiologist guarantees maintenance of the cold chain and equipment validation, providing the surgeon with a safe allograft ready for implantation (15).

Conclusion

The transfusiologist is not merely a supplier of blood components but a key clinical partner in transplantation and a guardian of the immunological gateway through high-resolution HLA typing and crossmatch testing, thereby directly preventing early organ rejection. The transfusiologist is also a manager of intraoperative survival, guiding the patient through severe hemostatic disorders and massive bleeding by means of point-of-care monitoring. Their expertise in immunogenetics, hemostasis control, and apheresis technologies represents a cornerstone of successful outcomes and patient survival. The long-term success of tissue and organ transplantation is a direct consequence of immunological safety and the precise perioperative support provided by the transfusiologist.

The transfusiologist is also the bearer of advanced technologies in therapeutic apheresis and tissue banking, enabling the management of postoperative complications and long-term tissue regeneration. The continuous development of transfusion medicine, the introduction of new molecular technologies, and automated apheresis systems guarantee further progress and a continued increase in survival rates among transplant patients.

In our setting, tissue and organ transplantation has still not been sufficiently established in relation to patients' needs. A particular problem for the development of this method is tissue and organ donation, which has not yet reached a satisfactory level. Therefore, despite the knowledge and experience already acquired, this treatment method cannot be applied without a sufficient number of tissue and organ donors.

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EXTRACORPOREAL PHOTOPHERESIS FOR THE TREATMENT OF GRAFT-VERSUS-HOST DISEASE

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Abstract

Graft-versus-host disease (GvHD) is severe immune mediated complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT). It is also the leading cause of mortality and decreased quality of life in transplanted patients. GvHD is caused by donor T cells that mediate host tissue damage via proinflammatory mechanisms. At the same time donor T cells also promote the graft-versus-tumor (GVT) effect, essential for the therapeutic efficacy of allo-HSCT. Acute GvHD (aGvHD) mainly affects the skin, gastrointestinal tract and liver. On the other hand, cGvHD imperfectly mimics other autoimmune disorders. Additionally, acute (aGvHD) has negative impact on immune reconstitution after allo-HSCT and is occured in the first three months and chronic (cGvHD) appears thereafter. Glucocorticosteroids are used as first-line therapy of GvHD, with introduction of ruxolitinib, imatinib, rituximab and other target agents as the second step in steroid refractory GVHD. Extracorporeal photopheresis (ECP) is used as an effective treatment for both steroid refractory aGvHD and cGvHD, combined with ruxolitinib, but its mechanisms remain incompletely understood. Data indicates that ECP normalizes the inverted CD4/CD8 ratio and increases the number of natural killer (NK) cells, shifts dendritic cell (DC) from DC1 to DC2 phenotype, and increases the T regulatory (Treg) lymphocytes.

Key words: extracorporeal photopheresis, allogeneic hematopoietic stem cell transplantation, graft versus host disease

Sažetak

Bolest kalema-protiv-domaćina (GvHD) je teška imunski posredovana komplikacija koja se javlja nakon alogene transplantacije matičnih ćelija hematopoeze (allo-HSCT). Ona je takođe i vodeći uzrok mrtaliteta i smanjenog kvaliteta života kod transplantiranih pacijenata.

GvHD je uzrokovan reakcijom kada donorske T ćelije posreduju u oštećenju tkiva domaćina putem proinflamatornih mehanizama. Istovremeno, donorske T ćelije takođe uzrokuju i reakciju kalema-protiv-tumora (GVT), što je neophodno za terapijsku efikasnost allo-HSCT. Akutni GvHD (aGvHD) uglavnom pogađa kožu, gastrointestinalni trakt i jetru. S druge strane, hronični (cGvHD) na određeni način oponaša različite autoimune poremećaje. Pored toga, aGvHD ima i negativan uticaj na imunsku rekonstituciju nakon allo-HSCT i javlja se u prva tri meseca, a cGvHD se javlja nakon toga. Glukokortikoidi se koriste kao terapija prve linije za GvHD, uz uvođenje ruksolitiniba, imatiniba, rituksimaba i drugih ciljnih agenasa koji predstavljaju naredni terapijski korak, kod steroidno refraktarnog GvHD. Ekstrakorporalna fotofereza (ECP) se koristi kao efikasan tretman kod steroidno refraktarnih oblika aGvHD i cGvHD, često u kombinaciji sa ruksolitinibom, ali mehanizmi kojim ECP deluje i dalje ostaju nedovoljno razjašnjeni. Ipak, pokazano je da ECP normalizuje odnos CD4/CD8 limfocita, povećava broj ćelija prirodnih ubica (NK), pomera dendritične ćelije (DC) sa DC1 na DC2 fenotip i povećava T regulatorne (Treg) limfocite.

Ključne reči: ekstrakorporalna fotofereza, alogena transplantacija hematopoetskih matičnih ćelija, bolest kalema protiv domaćina

Graft versus host disease as immune mediated complication after allogeneic hematopoietic stem cell transplantation

Acute and chronic graft-versus-host disease (aGvHD and cGvHD) as immune mediated complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT) represent the major causes of mortality, and late morbidity as well as reduced quality of life (1, 2).

GVHD is initiated by donor T cells that mediate host tissue harm via proinflammatory mechanisms. Simultaneously donor T cells also indorse the graft-versus-tumor (GVT) effect, crucial for the therapeutic efficacy of allo-HSCT. Thus, a key to a good recovery of the patients' after allo-HSCT lies on satisfactory immune recovery with the "right" balance of these two reactions.

Time frame for aGvHD is in the first three months and for cGvHD is therefore after allo-HSCT. But, this is not so strictly divided since there is a late occurrence of aGvHD, reccurent of persistent aGvHD. On contrary there is overlapped and classic cGvHD (3). Clinical presentations of aGvHD are skin, gastrointestinal tract and liver. Clinically, cGvHD imperfectly imitates other autoimmune disorders and is presented as multiorgan syndrome with inflammation and tissue fibrosis leading to constant organ dysfunction.

Corticosteroids are used as the first-line therapy to treat both aGvHD and cGvHD but non-responding patients (steroid refractory) require an additional immunosuppressive therapy and novel agents as ruxolitinib. Besides ruxolitinib therapeutical options includes imatinib, rituximab, mesenchymal stem cells, abatacept, vedolizumab, belomosudil, and other targeted drugs. Moreover, extracorporeal photopheresis (ECP) has shown its therapeutic efficacy, particularly in patients with cGvHD who failed corticosteroid treatments. Another potential benefit of ECP in the therapy of GvHD is that it improves GvHD while possibly preserving the GVT function (4). In steroid refractory aGvHD and cGvHD patients receive combined treatmant which include ruxolitinib and ECP, and this is defined as standard approach.

As a matter of fact, the cause of mortality is not GvHD *per se*, but are conditions associated with delayed immune reconstitution, poor graft function and effects of severe immunosuppressive therapy (IST).

High dose IST has been demonstrated to be a risk factor for amount of adverse effects, including infections and disease relapse. A significant strengths are being guided towards reducing systemic IST, but with attention on GvHD persistence. In this context ECP is positioned as a complementary treatment of GvHD which has been shown to provide immunoregulatory effects without increasing the risk of infectious (4).

In the setting of aGvHD there is delayed T cell reconstitution which is an essential step for a successful allo-HSCT outcome. There is a negative impact of GvHD and its first line treatment with corticosteroids on immune reconstitution, expecially CD4 T lymphocytes (5). Steroid-refractory disease often requires additional immunosuppressive agents creating a dangerous balance between controlling aGVHD and the risk of infection and relapse.

Extracorporeal photopheresis

ECP is a second-line, cell-based immunotherapy and well established immunomodulatory approach widely used for steroid-refractory aGVHD and cGvHD, with a good-recognised efficacy and safety profile (6–8). It works by processing and treating a patient's white blood cells with UVA light and a photosensitizer before re-infusing them in aim to modulate the immune response.

Together with successful GvHD treatment, ECP is able to provide a steroid-sparing effect, which is approved for the duration and quality of life of patients. The American Society of Apheresis (ASFA) recommends ECP as a second-line treatment for aGvHD stages II-IV, as well as in moderate - to severe - stage cGvHD (9).

ECP involves collection of peripheral blood mononuclear cells (PBMC) by apheresis, exposure to photosensitizer 8-methoxypsoralen (8-MOP), and ultraviolet A radiation, followed by re-infusion of photoactivated cells into the patient. Each cycle incudes the collection, separation and extracorporeal exposure of autologous white blood cells to 8-MOP and ultraviolet A radiation, with subsequent reinfusion.

Exclusively, there are no systemic immunosuppressive effects and ECP accelerates stopping of IST, thus acting in a manner not to increase risk of infection or disease relapse

Precisely how ECP exerts its therapeutic effects is not completely understood, but several mechanisms contributing to antigen-specific immunomodulation have been proposed including apoptosis of exposed lymphocytes, differentiation of monocytes into dendritic cells (DC) stimulated by physical interactions within the ECP chamber, promotion of a tolerogenic DC phenotype (shift od DC1 to Dc2) and increased regulatory T cells (Treg) although many studies incorporate *in vitro* ECP models or animal models (10). Retrospective studies also suggest that ECP can promote thymic-dependent T cell recovery after allo-HSCT.

Existing literature indicates that ECP normalizes the inverted CD4/CD8 ratio and increases the number of natural killer (NK) cells, shifts DC population from DC1 to DC2 phenotype, and increases the T regulatory (Treg) population (11, 12).

ECP timing and management strategy

Protocols for ECP timing and management strategy can be different among centers. In steroid refractory aGvHD (defined as refractorines on steroids 2mg/kg bw in period longer than 7 days) the goal is that it is better to start ECP as soon as possible combined with ruxolitinib.

ECP can be started in all patients with 2 (eventually 3) procedures *per* week. For aGvHD, standard therapy typically starts at 2 to 3 procedures per week on consecutive days for 4 weeks (13). For cGvHD, maintenance frequency generally begins at 1 to 2 procedures per week and than reduced over several months.

ECP in aGvHD

For steroid-refractory acute GvHD, ECP involves more frequent, strengthened scheduling to stop quick inflammatory responses (13).

The first phase of ECP in aGvHD is induction phase which is usually comprised of 3 treatments per week (sometimes for 2 consecutive days, or on alternating days) for the first 1 to 4 weeks.

If the response is favourable the next phase is continuation with tapering of ECP to 2 consecutive days per week for up to 3 months or until symptom resolve. Duration of ECP treatments typically rounds 4 to 6 months (13).

ECP in cGvHD

For cGvHD, ECP acts as an immunomodulatory therapy and is delivered on a less aggressive schedule, often over a longer time frame.

Treatment includes induction/maintenance phase which is usually consisted of 1 to 2 procedures consecutively per week (12, 13).

In the response is favourable the next approach is tapering phase when the frequency of ECP is gradually reduced to every two weeks, then to once every 3 to 4 weeks.

Duration of ECP can last 10 to 12 months or longer, and is typically tailored to the patient's steroid-sparing response and organ involvement.

Because ECP is highly individualized, exact protocols are frequently modified based on clinical response.

Comparison between inline and offline systems during ECP procedures

Generally, ECP is administered via two primary methods: inline (a single-step closed system) and offline (a two-step open process).

Inline (closed) system works as single dedicated device (such Theracos Cellex, Mallinckrodt plc; Amicus Blue, Fresenius Kabi) which performs the entire procedure - cell separation, drug incubation, photoactivation, and reinfusion - in one continuous, automated loop.

The advantages are that it takes less time, it is highly automated, and limits manual handling of the blood product. Inline system of ECP is optimal for patients with standard, adequate peripheral blood MNC counts and centers looking for operational simplicity.

Offline (open) system acts as standard apheresis device which first collects the MNCs. This collected concentrate is manually removed and transferred to a separate, specialized device for UVA irradiation and drug incubation of harvested MNCs. After that collected MNCs harvested by apheresis device like the Spectra Optia are transferred to MacoGenic G2 device and irradiated in *ex-vivo* conditions in combination with a photosensitizing agent 8-MOP. This irradiated product is than transferred to the patient.

The advantages of offline ECP are that it processes larger blood volumes, resulting in a much higher yield of target cells per cycle.

This ofline ECP system is better for patients with low MNC (such as children) or cases that require treating a larger number of cells per kg of body weight.

ECP traditionally delivered using either "inline" systems, which integrate MNC collection, photoactivation, and reinfusion to the patient, or "offline" platforms that allow greater processing flexibility, but require dedicated irradiation equipment. Access to separate UVA irradiators may be limited in clinical and research settings where cryopreservation of ECP-treated MNC is required.

In the study published by Castillo-Aleman et al (14), it was described a principle of a practical hybrid approach that adapts the inline Amicus Blue Photopheresis System into an inline-to-offline workflow, enabling larger total blood volume processing, partial reinfusion, and cryopreservation of photoactivated MNCs. Using a fixed 200-mL MNC collection,

followed by standard 8-MOP administration and UVA irradiation, 50 mL was reinfused inline, while the remaining cell product was aliquoted for offline cryopreservation. The mentioned method has been implemented in the OPERA clinical trial (NCT05413005) and conserves procedural safety, product integrity, and operational simplicity. The authors stated that this approach enables offline capabilities within an inline ECP framework without requiring an independent UVA irradiator and expands flexibility for clinical programs and translational research.

Assessing the response on ECP involves both overall clinical evaluation and specific organ scoring.

The efficacy of ECP - core assessment criteria

The initial efficiency evaluation of ECP can be made at four weeks, during which the absence of progression of GvHD manifestations must be determined. In cases of GvHD progression observed at this stage, the efficacy of ECP was admitted insufficient, and its continuation thought to be unwarranted.

The response to ECP therapy can be evaluated thereafter eight weeks. In the event of a complete, partial or minimal response, ECP procedures were continued in line with an individual plan, with a subsequent increase of time intervals between procedures (once a week, biweekly, etc.). If stabilization or progression of GvHD symptoms was noticed at 8 weeks from starting the ECP procedures, the treatment schedule was considered ineffective and the procedures were stopped. For patients with persistent GvHD and inadequate responses to ECP combined with IST, treatment typically transitions to alternative therapies like targeted JAK inhibitors (ruxolitinib) or other second-line agents, as ECP is often deemed ineffective in this setting (15).

Treatment response is typically evaluated at standardized intervals to determine the success of ECP (16).

The response in aGVHD is assessed clinically at the 1 - month mark, while in cGVHD it is generally assessed at 3 to 6 months, though improvements may take longer to manifest (17).

Classification of GvHD response after ECP

Clinicians utilize the standard NIH Consensus Criteria and scoring guidelines to classify the patient's status (17, 18). The classification of GvHD response after ECP can be assessed according to grade of regression of affecting organs or requirement for sparing steroid therapy. Those responses are listed as follows:

Complete response (CR): total resolution of all GvHD symptoms or complete regression of affected organs (eg. grade 0 -1 for aGvHD).

Partial response (PR): at least a 50% improvement in organ-specific involvement (eg., skin, gut, liver).

Stable disease (SD): less than 50% improvement or a requirement for reduced steroids with stable GvHD.

Progressive disease (PD): worsening of existing symptoms or the onset of new GvHD signs.

Furthermore, clinical consensus on ECP outcomes reveals several key findings, which are based on efficacy and response rates, as well as on steroid therapy sparing.

In this context efficacy and response rates are estimated for aGvHD and cGvHD, and for aGVHD the overall response rates of ECP shows generally ranging between 50% and 91%, particularly benefiting cutaneous and gastrointestinal manifestations. Moreover, for cGvHD studies report overall response rates ranging 50% to 70%, with the highest organ-specific improvements observed in the skin and oral mucosa (19, 20).

Concerning steroid-sparing effect after ECP, clinical data demonstrates that up to 65% to 87% of patients with steroid-refractory GvHD are able to significantly reduce or completely taper off their daily corticosteroid doses (21).

Take home messages and conclusions

Mechanism of ECP incudes its immunomodulatory action which induces apoptosis, prompting immune cells to secrete anti-inflammatory cytokines, upregulate Tregs, and reduce alloreactive T-cells without causing generalized immunosuppression.

The other important fact concerning ECP is favourable safety profile because ECP lacks systemic immunosuppressive side effects like widespread infection risk, which is highly suitable for heavily pre-treated patients who or have concurrent infections (22).

In steroid refractory aGvHD, ECP is an effective therapy in organs like the skin, liver, and gut. In this setting it also provides steroid-sparing effect, allowing patients to lower or discontinue corticosteroid use. Experts generally recommend an intensified schedule of 2 to 3 sessions per week during the first month, particularly for higher-grade (III–IV) aGvHD (23).

In steroid refractory cGvHD ECP is uniquely effective at treating fibrotic and sclerodermatous skin and joint manifestations. Complete response rates for cutaneous symptoms range from 70 - 80%. Clinical data shows improved response rates with

longer treatment duration since overall response rates jump significantly after 6 to 8 months of ECP. In this setting ECP induces durable responses, and when used in combination with other IST it improves failure-free survival rates (24).

Finally, ECP is a safe and highly effective second-line therapy for both steroid refractory aGVHD and cGvHD. It offers an excellent alternative to further systemic immunosuppression by actively promoting immune tolerance while retaining a potent steroid-sparing effect.

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BLOOD GROUP TERMINOLOGY: NEWS FROM THE ISBT WORKING PARTY

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Abstract

Many transfusion specialists may assume that most clinically relevant blood groups have already been discovered. Recent developments within the International Society of Blood Transfusion (ISBT) Working Party on Red Cell Immunogenetics and Blood Group Terminology (RCI&BGT) suggest otherwise. Between 2018 and May 2026, the number of recognized blood group systems increased from 36 to 48, reflecting continuing advances in serology, genomics, and membrane biology.

Importantly, however, modern blood group discovery is no longer confined to classical erythrocyte serology. Recent systems including CTL2, ER, MAL, CD36, EMM, and PIGZ demonstrate that blood group immunogenetics increasingly extends into previously "foreign territories" including neutrophil immunology, glycobiology, mechanosensory biology, developmental disorders, and broader human genetics.

At the same time, rapidly expanding genomic information increasingly challenges existing allele terminology systems. Nevertheless, current ISBT nomenclature remains highly effective for routine genotype interpretation and phenotype prediction. The future challenge may therefore no longer be the recognition of additional biological variation itself, but rather determining which variation is clinically meaningful enough to justify formal nomenclature.

Keywords: blood groups; genomics; ISBT terminology

Introduction

Many transfusion specialists may assume that most clinically relevant blood groups have already been discovered. Recent developments within the ISBT Working Party on Red Cell Immunogenetics and Blood Group Terminology suggest otherwise. Despite more than a century of investigation, blood group discovery remains surprisingly active (1, 2).

The ISBT currently maintains 12 Working Parties addressing different scientific and clinical aspects of transfusion medicine. Among them, the Working Party on Red Cell Immunogenetics and Blood Group Terminology (RCI&BGT) serves as the internationally recognized authority responsible for ratifying new blood group systems, antigens, and alleles. Between 2018 and the ISBT Congress in Kuala Lumpur in 2026, the Working Party was co-chaired by Catherine Hyland (Brisbane, Australia) and Christoph Gassner (Triesen, Liechtenstein). Since July 2026, the chair has been assumed by Margaret Keller (American Red Cross Blood Services, Philadelphia, USA).

During this eight-year period, membership increased from 22 to 37 international experts, while the number of recognized blood group systems expanded from 36 to 48. As of May 2026, the ISBT recognizes 48 blood group systems comprising 371 antigens. Including antigens assigned to the 200, 700, and 901 series, for which complete genetic characterization remains unresolved, nearly 400 blood group antigens are currently recognized (2).

From within the Working Party, one increasingly observes that modern blood group discovery is no longer confined to classical erythrocyte serology. Instead, blood group immunogenetics is increasingly extending into previously "foreign territories" including neutrophil immunology, glycobiology, membrane biology, developmental disorders, mechanotransduction, and broader human genetics.

Importantly, however, blood group terminology is ultimately not centered on systems themselves, but rather on the antigens that must be detected, interpreted, and considered during transfusion practice and pregnancy management. Although blood group systems provide the organizational framework for nomenclature, clinical transfusion medicine ultimately revolves around antigens, antibodies, and their biological and clinical consequences.

Ratification of Blood Group Systems

The Working Party evaluates candidate blood group systems and antigens according to internationally established criteria. One or more antigens may form a new blood group system if:

the antigen(s) are present on erythrocytes;

the antigen(s) are defined by human antibodies that are neither autoantibodies nor solely monoclonal antibodies;

the responsible gene has been identified and sequenced;

and the gene is different from, and not a closely linked homologue of, genes encoding antigens of existing blood group systems (1,2).

Recent years have additionally demonstrated that some antigens may be difficult to detect by standard hemagglutination methods and may instead require alternative technologies such as flow cytometry or mass spectrometry. Antigen expression on reticulocytes or earlier erythroid precursor stages, together with associated clinical consequences, may also be considered during evaluation of candidate systems.

These developments illustrate that modern blood group terminology increasingly reflects integrated serological, genomic, and functional characterization rather than classical serology alone.

Blood Groups Invading Foreign Territory

Several recently recognized blood group systems illustrate the changing biological landscape of immunohematology.

Particularly illustrative was the molecular resolution of the long-standing AnWj antigen through recognition of the MAL blood group system (ISBT 047). For decades, AnWj represented a clinically relevant but genetically unresolved antigen. Its eventual characterization demonstrates how modern genomic approaches continue to solve serological questions that remained unanswered for many years (2).

Particularly striking was characterization of the CTL2 blood group system (ISBT 039), in which the antithetical antigens Csa and Csb were shown to coincide molecularly with the HNA-3a/HNA-3b polymorphism known from neutrophil immunology. Consequently, boundaries between classical red cell serology and other branches of immunohematology are becoming increasingly blurred. In addition, the carrier gene *SLC44A2* has also been associated with hearing loss, further illustrating how blood group discoveries increasingly identify naturally occurring human “knock-out” models associated with mild hereditary disease (1).

Recognition of CD36 as blood group system 045 further demonstrates how blood group immunogenetics increasingly intersects with vascular biology, platelet biology, and inflammatory pathways extending well beyond erythrocytes themselves (2).

An emerging theme in modern blood group discovery is therefore that blood group antigens are no longer merely regarded as transfusion markers, but increasingly also as phenotypic indicators of subtle human genetic disease. Particularly illustrative are inherited glycosylphosphatidylinositol (GPI) deficiencies associated with the EMM blood group system. Homozygous defects in *PIGG* not only result in the rare Emm-negative blood phenotype but may additionally be associated with developmental and neurological abnormalities, thereby linking blood group discovery directly with inherited human disease (3).

Similarly, recognition of the ER blood group system (ISBT 044) provided molecular clarification for another historically recognized but incompletely understood serological specificity. Interestingly, the ER system is encoded by *PIEZO1*, a mechanosensitive ion channel gene recognized through the Nobel Prize-winning work of Ardem Patapoutian and colleagues. Thus, a classical blood group specificity unexpectedly intersected with one of the most fundamental recent discoveries in sensory and membrane biology (4).

The recently recognized PIGZ blood group system (ISBT 048) further extends these observations. Here again, blood group discovery intersected with free glycosylphosphatidylinositol biology, whole exome sequencing, flow cytometry, and functional genomics. At the time of writing, the formal Working Party report describing PIGZ has not yet been published.

Allele Terminology in the Genomic Era

The rapid development of next-generation sequencing technologies has fundamentally transformed blood group genetics. Increasingly comprehensive sequencing approaches now reveal enormous numbers of additional allelic variants across essentially all blood group systems. Consequently, existing allele terminology systems are increasingly challenged by the anticipated expansion of genomic information.

Within the field, discussions therefore periodically arise regarding the possible need for fundamentally revised nomenclature systems. Nevertheless, current ISBT allele terminology continues to provide a highly robust and clinically useful framework for routine genotype interpretation and phenotype prediction (5).

Until recently, ISBT blood group allele information was largely maintained in static PDF documents, typically one file per blood group system. While historically highly valuable, such formats increasingly became insufficient for the rapidly expanding complexity of blood group genomics.

Following several years of development, these data were transferred in November 2025 into a publicly accessible online database (https: //blooddatabase.isbtweb.org/), representing a major infrastructural transition for future blood group terminology and allele curation.

A nomenclature system that no longer assists clinical interpretation has failed its purpose. The goal of terminology is not maximal biological detail, but meaningful clinical communication. Complexity alone is not a scientific achievement.

For most blood group systems, currently recognized alleles are likely sufficient to predict the overwhelming majority of clinically relevant phenotypes encountered during routine blood group genotyping. The future challenge may therefore no longer be the recognition of additional biological variation itself, but rather determining which variation is clinically meaningful enough to justify formal nomenclature.

One possible future direction may involve increasingly structure-based interpretation of blood group variants. Recent in silico analyses of the highly polymorphic Kell blood group system demonstrated that three-dimensional protein modelling may help distinguish variants likely to alter antigenicity from those without clinically meaningful effects (6, 7). Such approaches may become increasingly important as genomic technologies continue to identify enormous numbers of previously uncharacterized alleles.

Clinical and Translational Perspectives

Modern blood group terminology increasingly intersects with translational molecular diagnostics. Non-invasive prenatal testing (NIPT) for fetal blood groups, particularly fetal *RHD* genotyping using cell-free fetal DNA, represents an important example of clinically implemented blood group genomics (8).

The growing integration of molecular blood group diagnostics into routine clinical care further emphasizes the importance of internationally standardized terminology, curated allele databases, and bioinformatic interpretation tools.

Conclusions

Recent developments within the ISBT Working Party on Red Cell Immunogenetics and Blood Group Terminology demonstrate that blood group discovery remains remarkably active despite more than a century of investigation. Modern blood group science increasingly integrates serology, genomics, immunology, glycobiology, membrane biology, and human genetics, thereby extending far beyond the traditional boundaries of erythrocyte serology alone.

From within the Working Party, one increasingly gains the impression that blood group systems are no longer merely classifications of erythrocyte antigens, but have become highly informative windows into broader aspects of human biology and disease.

The future challenge may therefore no longer be discovering additional blood group variation, but understanding which variation truly matters biologically and clinically.

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ESTABLISHING AN ANTI-D PLASMA COLLECTION PROGRAM IN EUROPE

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Abstract

Anti-D immunoglobulins (Ig) are essential for preventing haemolytic disease of the foetus and newborn caused by exposure to foetal RhD-positive erythrocytes during pregnancy/delivery, or immunisation after transfusion. Recently, the European Medicines Agency, the European Directorate for the Quality of Medicines & HealthCare (EDQM), and the European Blood Alliance (EBA) emphasised the importance of anti-D Ig as a critical medicinal product. They called for enhanced European resilience and reduced dependence on non-European sources for this product. The EBA and EDQM created an action plan to resume anti-D plasma collections across Europe. It involves setting technical requirements and establishing a large European plasma pool, rather than relying on smaller, separate national pools. In this context, the EDQM published a technical report, and a collaborative project between EBA and the BEST is underway. This collaboration focuses on quantifying and characterising blood donors who are naturally immunised against RhD, as well as assessing their potential mobilisation for non-profit anti-D plasma donation involving reimmunisation. Preliminary data indicate that such donors may provide a significant number of plasma donations in Europe, which, together with immunised non-blood donors and de novo immunised individuals, may create a donor pool that diminishes the vulnerability of the anti-D Ig supply.

Key words: Anti-D plasma, haemolytic disease of the foetus and newborn

Introduction

Haemolytic disease of the foetus and newborn (HDFN) occurs when an RhD-negative woman becomes alloimmunized after exposure to RhD-positive erythrocytes from her fetus during pregnancy/delivery or from a previous transfusion. These antibodies may cross the placenta in subsequent pregnancies and destroy fetal RhD-positive erythrocytes, causing fetal anaemia, which can lead to severe hydrops fetalis and, if untreated, severe hyperbilirubinemia and kernicterus post-birth. RhD-mediated HDFN is preventable by anti-D immunoglobulins (Ig). Before 1945, HDFN had a 50% mortality rate. Advances in diagnostics, intrauterine transfusions, and prophylaxis with polyclonal anti-D Ig since 1968 have nearly eradicated HDFN in high-income countries. In Australia, deaths dropped from over 1 per 1,000 births in the 1960s to 1 per 100,000 three decades later (1]. Using both antenatal and postpartum immunoprophylaxis with anti-D Ig is more than 99% effective in preventing maternal sensitisation to the RhD antigen (2).

Anti-D immunoglobulins

Polyclonal anti-D Ig are produced from the plasma of RhD-negative donors, immunised with RhD-positive erythrocytes, either deliberately or during pregnancy, or rarely, natural carriers of anti-D without prior exposure. Donors need antibody levels >45 IU/ml (approximately 1: 512 titre), which requires restimulation with RhD-positive erythrocytes. As the number of previously immunised individuals decreases, most anti-D plasma now comes from hyperimmunized naïve donors. The donated anti-D plasma is pooled, IgG antibodies are purified, and pathogens are removed/inactivated. The plasma pool should hold at least 250 litres of plasma; however, in practice, it exceeds 3,000 litres to facilitate more cost-effective purification.

Anti-D Ig mainly eliminates fetal red blood cells before they trigger an immune response, but antigen modulation and other effects also play a role (3). To prevent HDFN, RhD-negative pregnant women are identified early, then given anti-D Ig at 28 GW or in two doses at 28 and 34 GW, and postpartum within 72 hours or after pregnancy termination. An extra dose is given after sensitising events. *RHD* fetal genotyping on maternal blood allows immunoprophylaxis only for RhD-negative women with RhD-positive fetuses, about 60% of cases in Western populations (4).

In Europe, anti-D Ig is classified as a critical medicine, whose shortages could cause serious harm or pose significant risks to patients (5). Existing alternatives, however, have limitations: the efficacy of monoclonal anti-D Ig remains un-

certain, whereas FcRn inhibitors carry a potential risk of maternal and foetal agammaglobulinaemia and are not widely accessible (6). Therefore, the focus remains on polyclonal anti-D immunoprophylaxis.

Challenges in the supply of anti-D Ig

Worldwide data show that low-income countries have limited access to anti-D products, and only 50% of women in need receive prophylaxis worldwide (7). In response to these ongoing challenges associated with Rh disease, a multidisciplinary international organisation, the Worldwide Initiative for Rh Disease Eradication (WiRhE), was established in 2019. WiRhE's mission is to eliminate Rh disease by 'connecting the world to protect mothers and babies' (8).

A comprehensive overview of the management strategies for HDFN prevention across various European nations was published in 2021 (9). The European Directorate for the Quality of Medicines & HealthCare (EDQM) organised three webinars in 2023 to raise awareness about the challenges in anti-D Ig supply. The webinars discussed the collection of anti-D plasma, the production of anti-D IgG products, and possible solutions, including the development and use of alternative and complementary anti-D products.

As global anti-D plasma collections are mainly concentrated in the USA, during the COVID-19 pandemic, there was a 25% decrease in the availability of anti-D plasma and, consequently, related products. Based on information about IgG anti-D shortages in the USA posted by the FDA in December 2023 (9), the AABB published an Association Bulletin #24-02, titled "Use of Rh Immune Globulin and Considerations in the Setting of Supply Shortages and Limited Availability(10)." This shortage was attributable to factors impacting the anti-D plasma market as well as manufacturing deviations. Initially, it involved a single United States manufacturer; however, it has since expanded to include other IgG anti-D manufacturers. Given that the majority of the world's anti-D plasma is collected in the United States and that U.S. producers supply products internationally, shortages could affect the availability of IgG anti-D products beyond the United States, including in Europe. Additionally, The Business Research Company's 2025 Global Market Report predicts robust growth for the anti-D immunoglobulin market in the coming years (11), indicating increased demand that could contribute to global shortages.

Securing a sustainable supply of anti-D Ig in Europe.

EBA/EDQM survey

In 2025, the EBA and EDQM established an action group to conduct a survey exploring the collection of anti-D plasma in Europe. The questionnaire was distributed to members of the EBA and EDQM. The survey period was between 30. 10 2024, to 6.12 2024. Responses from 19 European countries indicated response rates of 59% for the EU (16 of 27 countries), 53% for the EU/EEA (16 of 30 countries), and 49% for the Council of Europe (19 of 39 countries). None of the surveyed countries has a program for collecting anti-D-specific plasma. Small quantities are collected in Poland and Ukraine, covering around 2% of European needs. Most European countries ceased their collection during the 1980s and 1990s. The Netherlands stopped in 2020. The reasons for this discontinuation lie in the gradual withdrawal of plasma fractionation companies from anti-D plasma collection in Europe, economic considerations, and the decline in immunised donors due to successful immunoprophylaxis. However, there is interest in starting or restarting anti-D plasma collection in several European countries, while others remain undecided. Only a few blood establishments would not consider collecting such plasma. Countries that previously had anti-D plasma collection programs are more likely to consider restarting them. The main obstacles to starting anti-D plasma collections include issues related to plasma donors, costs, and various organisational and regulatory challenges (12). Key challenges in plasma donation include the declining number of immunised donors, the potential need to immunise new donors, and the difficulty of collecting small batches of anti-D plasma for fractionation.

EMA recommendation

The European Medicines Agency (EMA) responded to the reported shortages of anti-D IgG in the United States by issuing recommendations from the Executive Steering Group on Shortages and Safety of Medicinal Products (13). It underscores Europe's vulnerability due to its reliance on imported anti-D products, predominantly derived from plasma collected in the United States, alongside global supply capacity constraints involving a limited number of Marketing Authorisation Holders and plasma collection centres for anti-D Ig manufacture. Consequently, shortages within the United States may influence the supply chain in Europe. Additionally, the limited number of immunised donors and a decline in the pool of existing donors, coupled with challenges related to the collection, manufacturing, and pooling of small plasma batches, are of concern. The EMA thus advised member states to recommence anti-D plasma collection efforts.

Action plan and activities for sustained anti-D Ig supply across Europe

The EBA and EDQM discussed a potential approach to ensure a steady supply of anti-D Ig throughout Europe, framing it as a strategic matter of health sovereignty that calls for coordinated, ongoing efforts at the European level. Consequently, they have launched an ambitious action plan that includes (14):

Developing a comprehensive roadmap to (re)initiate anti-D plasma collection in Europe, outlining best practices for screening, immunisation, and collection. This will likely necessitate both de novo and repeat immunisation, requiring strict safety and ethical oversight.

Ensuring dedicated financial support from the EU member states and the European Commission is required.

Establishing a European pooling model to enable the fractionation of anti-D plasma batches collected from multiple Member States.

Enhancing the implementation of fetal *RHD* genotyping to guide antenatal immunoprophylaxis.

Investigating whether anti-D dosing can be reduced.

Supporting the development of antibody alternatives by encouraging relevant research through dedicated funds.

In 2026, the EDQM/CD-P-TS issued a comprehensive technical report consolidating the outcomes of recent initiatives and activities. This report complements the EMA MSSG recommendations by providing essential technical context to facilitate their implementation. It emphasises scientific, technical, regulatory, and operational considerations to support the development of European anti-D plasma collection programs. The primary objective of the report is to inform and support efforts to (re-) establish coordinated and sustainable anti-D plasma collection across European member states (12).

Discussions with several fractionators showed their support for developing a shared "European" batch of anti-D plasma. They did not see any barriers to fractionating anti-D plasma from unpaid donations as part of a feasible business model. They highlighted the timeliness of the initiative amid high global demand for anti-D plasma and shared positive experiences from Australia, where anti-D plasma has been successfully fractionated from unpaid donors. Additionally, they stressed the importance of securing backing from European and national regulators, as well as public health organisations, to create a sustainable system for collecting and producing this common anti-D plasma batch.

Based on data from 2023 and a model described in the literature (7), it has been estimated that the EU member states would require approximately 1750 units of donated anti-D plasma per one million inhabitants to sufficiently meet the demands for antenatal and prenatal immunoprophylaxis with anti-D Ig, while taking into account foetal *RHD* genotyping to inform antenatal applications.

EBA / BEST Anti-D Plasma Donor Project - AD-DONOR project

The EBA / BEST Anti-D Plasma Donor Project, or AD-DONOR, was initiated in February 2026 to promote sustainable self-sufficiency in anti-D plasma. Its goal is to gather strong evidence on the size, characteristics, and feasibility of mobilising the anti-D immunised blood donor pool. Any strategy to increase anti-D plasma availability must be ethical, operationally viable, and evidence-based. A key challenge is understanding the potential donor base: individuals who have developed anti-D alloimmunisation, often after pregnancy or transfusion. These donors are present in all blood services, but they are not systematically quantified, and the processes for detection, confirmation, counselling, and retention vary significantly. Consequently, the actual "recoverable" anti-D donor pool remains unknown, and planning based on assumptions rather than data could lead to inaccurate projections.

The project started with a basic step: understanding the number and key traits of blood donors with anti-D immunisation, using minimal data across blood establishments. This mapping will determine feasibility and scale. It helps decide on investment and the organisation of collection sites by estimating how many donors are anti-D immunised and eligible for plasmapheresis. Starting with a retrospective, aggregated study provides a low-risk approach aligned with data minimisation. Once the pathways are understood, a second phase will assess anti-D–immunised donors by examining their immunological profiles, the stability of anti-D antibodies, risk factors, sensitisation history, and willingness to participate in donation programs. This phase will also explore the feasibility of (re)immunisation strategies to maintain antibody levels for plasma collection, which will require ethical justification, risk–benefit analysis, informed consent, and oversight. Another BEST project on anti-red blood cell (anti-RBC) immunisation in blood donors is underway. While the objectives differ, both projects need data on donors who have been immunised with anti-D. Efforts are being made to coordinate study designs, prevent data duplication, and enhance project complementarity.

Initial results from the first phase of the project indicate that naturally immunised donors could contribute a substantial amount of anti-D plasma donations. However, this does not guarantee self-sufficiency in the supply of anti-D Ig. In addition to naturally immunised non-blood donors, *de novo* immunisation strategies might also be necessary.

Future steps

The current activities are the first step toward restarting anti-D plasma collections in Europe. While awaiting the results of the ongoing related studies, it is anticipated that efforts will be made to specify the regulatory framework, address ethical concerns regarding donor immunisation, and outline the technical aspects of preparing a common EU batch of anti-D plasma for fractionation. Additionally, identifying funding sources at the EU level is expected. These initiatives will precede the formation of a consortium of interested blood establishments to discuss resuming anti-D plasma collections by creating an anti-D plasma donor pool and reducing dependence on anti-D Ig supply across Europe.

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ANTITHROMBIN DEFICIENCY - DIAGNOSTIC AND THERAPEUTIC APPROACH

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Abstract

Antithrombin (AT) deficiency represents one of the most severe inherited thrombophilias. Although it is considered a rare disorder, available knowledge suggests that AT deficiency is underestimated due to the limitations of current diagnostic algorithms. Another cause of underdiagnosis is the high clinical variability of this patient population. Heterozygous type I-AT deficiency are normally associated with a severe thrombophilic phenotype. Heterozygous type II-AT deficiency are heterogeneous, considered as mild/moderate and the most prevalent. Antithrombin Budapest 3 (p.Leu131Phe) is the most frequent type II in Europe, particularly in the Roma population, with a remarkable existence of homozygous subjects. Carriers of this mutation have a very low AT activity (< 20%). They, tend to have juvenile/recurrent VTE and numerous issues that one might encounter when treating this patients. Also, in patients with AT deficiency (Budapest 3 homozygous) all types of obstetrical complications such as pregnancy related thrombosis, repeat fetal loss, intrauterine growth restriction and preeclampsia have been recorded. While, type I is associated mostly with high risk of pregnancy related thrombosis. Timely made diagnosis is cornerstone in the therapeutic approach, relation to the anticoagulant therapy selection and assessment of the length of its application after the appearance of the first thrombotic event.

Key words: Antithrombin deficiency, diagnostic methods, therapeutic approach

Sažetak

Nedostatak antitrombina (AT) predstavlja jednu od najtežih naslednih trombofilija. Iako se smatra retkim poremećajem, dostupna znanja ukazuju na to da je nedostatak AT potcenjen zbog ograničenja trenutnih dijagnostičkih algoritama. Još jedan uzrok nedovoljne dijagnoze je visoka klinička varijabilnost ove populacije pacijenata. Heterozigotni nedostatak tipa I-AT je obično povezan sa teškim trombofilnim fenotipom. Heterozigotni nedostatak tipa II-AT je heterogen, smatra se blagim/umerenim i najrasprostranjenijim. Antitrombin *Budapest* 3 (*p.Leu131Phe*) je najčešći tip II u Evropi, posebno u romskoj populaciji, sa značajnim prisustvom homozigotnih nosilaca. Nosioci ove mutacije imaju veoma nisku aktivnost AT (< 20%). Oni imaju tendenciju da imaju juvenilnu/rekurentnu vensku tromboemboliju (VTE) i brojne probleme sa kojima se možemo suočiti prilikom lečenja ovih pacijenata. Takođe, kod pacijenata sa nedostatkom AT (*Budapest* 3 homozigot) zabeležene su sve vrste akušerskih komplikacija kao što su tromboza povezana sa trudnoćom, ponovljeni gubitak fetusa, intrauterino zaostajanje rasta i preeklampsija, dok je tip I uglavnom povezan sa visokim rizikom od tromboze povezane sa trudnoćom. Blagovremeno postavljena dijagnoza je temelj terapijskog pristupa, odnosno izbora antikoagulantne terapije i procene dužine njene primene nakon pojave prvog trombotičnog događaja.

Introduction

Antithrombin (AT) is the most important physiological anticoagulants who play important and well known roles in the haemostatic system. However, recently more novel roles of AT have been discovered (1). This review aims to outline new roles of AT as well as diagnostic and therapeutic approach in those patients who were diagnosed to have AT deficiency. Timely diagnosis of AT deficiency, by applying a sufficiently sensitive tests during evaluation of biological activity, could have a significant implication on the further course and clinical presentation of this severe thrombophilia type.

AT- function

In addition to the already known role in neutralization of many coagulation enzymes including: thrombin, plasmin, and factors IXa, Xa, XIa, XIIa, there is the report about pivotal role of AT in mediating anticoagulation and anti-inflammatory effects (1). AT levels can be lowered in systemic inflammatory diseases. The reason for this decline is consumption by the coagulation system but also by immunological processes (2). Namely, cytokines as inflammatory mediators, promote

the expression of tissue factor (TF), on cell surfaces, causing activation of coagulation. At the same time, physiological anticoagulants, including AT, TFPI, and the PC system, are suppressed. This suppression can lead to an uncontrolled coagulation and inflammation, causing to disseminated intravascular coagulation (DIK), that contributing to development of multiple organ dysfunction especially in septic patients (3). On the other hand, AT causes distinct anti-inflammatory signaling responses. It binds to structures of the glycocalyx (syndecan-4) and further modulates the inflammatory response of endothelial cells and leukocytes by interacting with surface receptors. Additionally, AT exerts direct antimicrobial effects, namely depending on AT glycosylation it can bind to and perforate bacterial cell walls (2). AT has also been implicated in angiogenesis and its in vivo angiogenic and antitumor activity provides evidence that the clotting and fibrinolytic pathways are directly related to the regulation of angiogenesis (4,5). Both anti-inflammatory and antiangiogenic/proapoptotic properties of AT are shown to be mediated through interaction of the same D-helix of the serpin with heparan sulfate proteoglycans (HSPGs) on vascular endothelial cells. While, the protease inhibitory activity of AT is mediated by binding to the active-site of coagulation proteases through an exposed and mobile reactive center loop (RCL) (5). Inherited AT deficiency, caused by SERPINC1 gene mutations, plays important role in development arterial and venous thrombosis (deep venous thrombosis and/or pulmonary embolism, thrombosis of unusual sites); obstetrical complications (pregnancy related thrombosis, repeat fetal loss, intrauterine growth restriction and preeclampsia) (6,7). While, organ transplantation and ischemia/reperfusion, cardiac surgery with cardiopulmonary bypass, extracorporeal membrane oxygenation (ECMO), treatment with L-asparaginase and sepsis/DIK are the most common diseases or conditions that lead to acquired AT deficiency (8).

Inherited AT deficiency – clinical presentation

Antithrombin deficiency represents one of the most severe inherited thrombophilias. AT deficiency - heterozygous type I (quantitative variants) are commonly associated with the classic thrombophilic phenotype ie, juvenile thrombosis, idiopathic, and recurrent venous thromboembolism (VTE) events. Conversely, heterozygous type II (qualitative variants) have a more heterogeneous clinical presentation. Three subcategories are distinguished in this type: reactive site (RS), heparin-binding site (HBS), and pleiotropic effect (PE) (9). AT Budapest 3 (c.391C>T, p.Leu131Phe) is a type II-HBS variant with founder-effect origin in the Roma population (9,10). Specifically, while most SERPINC1 variants are caused by private mutations found in a single family, ATB Budapest 3 can be detected worldwide. This variant represents about 30% of cases with AT deficiency in large European cohorts. AT Budapest 3 homozygous individuals makes this mutation highly remarkable. In carriers of this mutation a very low AT activity (lover than 20%) is often recorded. They, tend to have juvenile/recurrent VTE and numerous issues that one might encounter when treating patients with AT deficiency (10). Also, in patients with AT deficiency (Budapest 3 homozygous) all types of obstetrical complications such as pregnancy related thrombosis, repeat fetal loss, intrauterine growth restriction and preeclampsia have been recorded), while type I is associated mostly with high risk of pregnancy related thrombosis (6, 11).

According to the literary data patients with AT deficiency, have an estimated annual thrombotic risk of 2.3%, about half of VTEs events developed before <40 years, while nearly another half are unprovoked (12). Deep venous thrombosis (DVT) of lower limb, that could be complicated with pulmonary embolism (PE), is the most frequent manifestation observed in75%, but thrombosis can also develop in atypical places such as, abdominal thrombosis, upper limb, or arterial thrombotic events that have been reported, particularly in subjects with type II variants (10,13).

Diagnostic approach

The current ISTH recommendations (8) for clinical laboratory testing for AT deficiency specify the initial test for AT deficiency is a chromogenic activity (functional) assay with heparin. They recommend a short incubation time of 30 seconds, unless reagents are proven to detect heparin binding site mutations with a longer incubation time. If the result of the functional assay is decreased, they recommend an antigen assay to determine the type/subtype of AT deficiency. The authors indicate that genetic testing helps detect particular deficiencies such as AT Dublin (p.Val30Glu), AT Wibble (p.Thr117Met), and AT Rouen VI (p.Asn219Asp), that can have normal results for both activity and antigen (8). Also we have to note that the use of antigen assay alone implies that Type II antithrombin deficient patients will not be identified (14). Bearing in mind everything mentioned above, there is widespread failure to follow the ISTH recommendations on how to diagnose antithrombin deficiency so cases will be missed.

In our population the genotyping results confirmed that the patients with lowest AT level activity with severe clinical presentation (juvenile thrombosis events, spontaneous recurrent thrombosis, abdominal and arterial thrombosis and all obstetrical complications) were the carriers of type-II HBS AT deficiency (Budapest 3-homozygous mutation) (6,13). We have to note that the complexity of type-II HBS AT deficiency diagnosis, showing the importance of apply sufficiently enough sensitive assay during measurement of functional AT level, while genetic analyses could defined subtypes of type II HBS, that is extremely important in those who are carriers of Budapest 3-homozygous mutation. Genetic testing and use of

enough sensitive assay for AT measurement influenced on increase in detection of AT deficiency patients in our population from 0.2% to 2.48%.

Therapeutic approach

Considering the importance of AT role, it is very significant to make timely diagnosis of AT deficiency. This is cornerstone in the therapeutic approach relation to the selection of anticoagulant therapy type as well as the assessment of the length of its application after the appearance of the first thrombotic event. That could have a significant implication on the further course and clinical presentation of this severe thrombophilia type (15)

Considering that AT deficient patients have a greater risk of recurrent VTE (odds ratio: 2.1; 95% CI: 0.2-4.0) (12), this risk supports long-term anticoagulation, particularly for heterozygous type I and homozygous type II patients (Budapest 3). Currently, there is no high-quality evidence in the case of heterozygous type II variants, the decision should be individualized in relation to the other risk factors such as age, obesity comorbid diseases. So, the choice of the oral anticoagulant should also be considered on a case-by-case basis. The efficacy and safety of direct oral anticoagulants (DOACs) for treatment of venous thromboembolism (VTE) in patients with thrombophilia was evaluated in several studies showing that VTE recurrence rate and all bleeding events were similar among all types of thrombophilia patients who were treated with DOACs compared to vitamin K antagonists (VKA). A review of recently published ISTH SSC communication (15) suggests that full-dose DOACs have similar efficacy and bleeding rates to VKAs in most individuals with severe thrombophilia. However, this recent ISTH SSC communication pointed to the observations from several studies of severe thrombophilia (e.g., Protein S (PS) and antithrombin (AT) Type II HBS (homozygous Budapest 3)), that indicate treatment failures in this specific group of patients treated with direct Factor Xa inhibitors. They recommended caution in using DOACs in those patients based on evidence of limited efficacy (15). Based on the current knowledge, an individual therapeutic approach relying on clinical judgment and experience seems reasonable when tailoring anticoagulant therapy for patients with severe inherited thrombophilia, including AT deficiency (10,15).

AT concentrates in the thromboprophylaxis and treatment of VTE in AT deficient patients

Plasma derivatives and recombinant products are 2 types of AT concentrates which can be used for supplementation. They are approved for thromboprophylaxis of VTE in AT deficient patients. However, only the plasma derivative concentrate has been approved for VTE treatment. Clinical data suggest that, even in supraphysiological doses, AT concentrates are safe. While, severe hemorrhagic episodes have been reported in lover than 5% of patients, particularly when AT concentrates are combined with heparin. So, when using AT concentrates, heparin adjustments guided by laboratory assays (anti-Xa) and clinical monitoring are recommended (10).

The clinical issues associated with the pregnancy in woman with AT deficiency are still mostly unresolved (11). Two types of clinical presentation can be recognized in this setting. There is a high risk of maternal thrombosis. In the treatment of thrombosis anti–FXa-adjusted therapeutic dose LMWH is advisable, and AT concentrates can also be useful (10). Pregnant women should be carefully monitored since thrombosis might still occur despite treatment. Also, there are increased risk for obstetric complications (eg, recurrent pregnancy losses, intrauterine growth retardation, and preeclampsia), and adverse pregnancy outcomes may also be one of the first symptoms in these patients. We have to note that successful pregnancies (mostly preterm deliveries) in pregnant women carriers of Budapest 3 homozygous variant, have been only observed under anticoagulation, and despite treatment, the risk of miscarriage/stillbirth remains very high (6,11).

To date, we do not have a guideline for the treatment of pregnant women with AT deficiency. So far, small series or case reports have been presented, so there is still not enough reliable evidence to make a recommendation. Expert proposals on the optimal management of these controversial areas, and future investigation are necessary.

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TRAUMA-INDUCED COAGULOPATHY

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Abstract

Trauma-induced coagulopathy (TIC) is a complex hemostatic disorder that develops early after severe trauma and significantly contributes to increased mortality and morbidity in injured patients. TIC is associated with higher transfusion requirements, increased incidence of multiple organ dysfunction, and poorer clinical outcomes. Its pathogenesis involves a complex interaction of tissue injury, hypoperfusion, inflammatory response, platelet dysfunction, hyperfibrinolysis, and endothelial damage. Additional factors contributing to coagulopathy include hypothermia, acidosis, and hemodilution, collectively known as the "lethal triad" of trauma. Contemporary management relies on early recognition using conventional coagulation assays and viscoelastic testing, followed by prompt implementation of targeted hemostatic and transfusion therapy. The aim of this review is to summarize current knowledge regarding the pathophysiology, diagnosis, and management of trauma-induced coagulopathy, with particular emphasis on the role of transfusion medicine.

Keywords: trauma-induced coagulopathy; massive hemorrhage; transfusion

Sažetak

Traumom indukovana koagulopatija (TIC) predstavlja kompleksan poremećaj hemostaze koji se razvija neposredno nakon teške traume i značajno doprinosi povećanom mortalitetu i morbiditetu traumatizovanih pacijenata. Prisustvo TIC povezano je sa povećanom potrebom za transfuzijskim lečenjem, češćim razvojem multiorganske disfunkcije i lošijim kliničkim ishodom. Nastanak ovog poremećaja uslovljen je složenom interakcijom hipoperfuzije, oštećenja tkiva, inflamatornog odgovora, poremećaja funkcije trombocita, aktivacije fibrinolize i endotelne disfunkcije. Dodatni doprinos razvoju koagulopatije imaju hipotermija, acidoza i hemodilucija, poznate kao „letalna trijada traume". Savremeni pristup podrazumeva rano prepoznavanje poremećaja koagulacije primenom standardnih laboratorijskih i viskoelastičnih testova, kao i pravovremenu primenu ciljane hemostatske i transfuzijske terapije. Cilj ovog rada je prikaz savremenih saznanja o patofiziologiji, dijagnostici i lečenju traumom indukovane koagulopatije sa posebnim osvrtom na značaj transfuzijske medicine.

Ključne reči: traumom indukovana koagulopatija; masivno krvarenje; transfuzija

Introduction

Trauma is one of the leading causes of mortality worldwide, accounting for approximately 8% of all global deaths, with an estimated 4.5 million deaths annually (1). According to the 2014 Berlin definition, polytrauma is defined as injuries involving at least two body regions with an Abbreviated Injury Scale (AIS) score ≥3, accompanied by at least one of the following physiological abnormalities: hypotension (systolic blood pressure ≤90 mmHg), impaired level of consciousness (Glasgow Coma Scale [GCS] ≤8), acidosis (base deficit ≤−6 mmol/L), coagulopathy (INR ≥1.4 or aPTT ≥40 s), or age ≥70 years (2).

Trauma-induced coagulopathy (TIC) is a common complication of severe trauma and has been recognized as an independent predictor of mortality, irrespective of the presence of other risk factors. Its presence is associated with an increased risk of complications, greater requirements for transfusion of blood components, and poorer clinical outcomes (3,4).

Despite substantial advances in prehospital care, surgical techniques, transfusion therapy, and intensive care, mortality and morbidity among severely injured patients remain high (5). The pathophysiological mechanisms underlying TIC have

not yet been fully clarified, while the optimal approach to its diagnosis, treatment, and monitoring remains the subject of extensive research. Therefore, early recognition of coagulation abnormalities is crucial for the timely implementation of appropriate therapeutic interventions and improvement of clinical outcomes (6).

Pathophysiology Of Trauma-Induced Coagulopathy

The etiology of coagulopathy in trauma patients is multifactorial and involves the interaction of several mechanisms that are activated immediately after injury or during subsequent treatment. The severity of coagulation abnormalities depends both on the characteristics of the injury itself and on external factors and therapeutic interventions. Prehospital administration of large volumes of crystalloid solutions, prolonged tissue hypoperfusion, hypothermia, and metabolic acidosis are important triggers for the development and progression of TIC (7). Unlike most traumatic bleeding, in which blood loss can be controlled by mechanical measures such as compression, embolization, or surgical repair of the injured blood vessel, TIC is characterized by impaired formation and stabilization of the blood clot, including at the level of the microcirculation. This results in diffuse bleeding, which may occur even at sites not directly affected by the traumatic injury (8). Physiological hemostasis depends on a dynamic balance between coagulation and fibrinolysis, allowing effective control of bleeding while simultaneously preventing unwanted intravascular thrombosis. Disruption of this balance leads to coagulopathy, with an important contribution from factors traditionally described as the “lethal triad of trauma”: acidosis, hypothermia, and hemodilution. Acidosis develops as a consequence of tissue hypoperfusion and shock, hypothermia results from environmental exposure and the administration of cold intravenous fluids, whereas hemodilution develops following fluid resuscitation and transfusion of blood products with insufficient concentrations of coagulation factors. In addition, some patients may develop disseminated intravascular coagulation (DIC), representing a manifestation of systemic activation and consumption of coagulation factors. Unlike DIC, trauma-induced coagulopathy represents a complex biochemical response to injury and hemorrhagic shock mediated by dysregulation of the coagulation cascade, abnormal fibrinolysis, endothelial dysfunction, activation of the inflammatory response, and systemic platelet dysfunction (9). Together, these mechanisms contribute to uncontrolled hemorrhage, progression of shock, and an increased risk of death in severely injured patients.

Contemporary research suggests that TIC represents a specific endogenous response to trauma and shock. Proposed mechanisms include activation of the protein C pathway, endothelial dysfunction, hyperfibrinolysis, platelet dysfunction, and consumption of coagulation factors. The development of coagulopathy is further aggravated by hypothermia, acidosis, and hemodilution (10-12).

Contemporary Diagnostic Approach

In addition to conventional laboratory parameters, the contemporary assessment of coagulation in trauma patients increasingly relies on point-of-care testing. Viscoelastic methods, such as thromboelastography (TEG) and rotational thromboelastometry (ROTEM), provide rapid and comprehensive assessment of the coagulation process, from initial clot formation through clot stabilization to fibrinolysis. Unlike conventional coagulation tests, which assess individual components of the coagulation cascade, viscoelastic methods enable real-time evaluation of clot formation, clot strength and stability, the contribution of platelets and fibrinogen, and the presence of hyperfibrinolysis.

A major advantage of these methods is their ability to facilitate individualized treatment. Based on TEG or ROTEM findings, fibrinogen, platelets, plasma, or antifibrinolytic agents can be administered in a targeted manner, thereby reducing unnecessary use of blood components and the associated risk of transfusion-related complications. Numerous studies have demonstrated that viscoelastic-guided treatment protocols may reduce blood component utilization, shorten intensive care unit length of stay, and improve survival among trauma patients (13-15).

Damage Control Resuscitation

The concept of damage control resuscitation (DCR) was developed with the aim of interrupting the vicious cycle of hemorrhage, hypothermia, acidosis, and coagulopathy. The fundamental principles of this approach include rapid control of the bleeding source, restrictive administration of crystalloid solutions, permissive hypotension in selected patients, and early administration of blood components.

Excessive administration of crystalloid solutions may lead to hemodilution, tissue edema, and worsening of coagulopathy. Contemporary guidelines therefore recommend limiting crystalloid administration while introducing blood components and hemostatic agents early in the course of resuscitation. The objective is to maintain adequate tissue perfusion while avoiding exacerbation of ongoing hemorrhage.

Role of Fibrinogen

Fibrinogen plays a central role in the formation of a stable blood clot. During massive hemorrhage, fibrinogen concentrations decrease rapidly, often before clinically significant reductions in other coagulation factors occur. Low fibrinogen levels are associated with increased mortality and greater transfusion requirements.

Contemporary European guidelines recommend maintaining fibrinogen concentrations above 1.5-2.0 g/L in patients with severe traumatic bleeding. Hypofibrinogenemia may be corrected using fibrinogen concentrate or cryoprecipitate, with fibrinogen concentrate allowing more rapid and precise replacement (11).

Tranexamic Acid

Tranexamic acid is a synthetic antifibrinolytic agent that inhibits fibrin clot breakdown. Results from the large multicenter CRASH-2 trial demonstrated that early administration of tranexamic acid significantly reduces mortality due to bleeding in trauma patients (10).

The greatest benefit is achieved when tranexamic acid is administered within the first three hours following injury. The standard regimen consists of an initial dose of 1 g administered intravenously over 10 minutes, followed by an infusion of 1 g over the subsequent eight hours. Owing to its demonstrated efficacy, tranexamic acid has become an integral component of contemporary management protocols for trauma patients with significant hemorrhage.

Future Directions

Although substantial progress has been made in recent years in understanding trauma-induced coagulopathy, numerous questions remain unresolved. Future research is focused on identifying biomarkers that may facilitate earlier recognition of hemostatic abnormalities and on developing personalized therapeutic strategies based on individual patient characteristics.

The increasing use of viscoelastic testing, coagulation factor concentrates, and targeted hemostatic therapy suggests that the future management of trauma-induced coagulopathy will increasingly rely on precision medicine and an individualized approach to each patient.

Transfusion Therapy

Early and appropriate transfusion therapy represents a cornerstone of contemporary management. Massive transfusion protocols involve balanced replacement with red blood cells, fresh frozen plasma, and platelets. Particular emphasis is placed on early administration of tranexamic acid and correction of hypofibrinogenemia with fibrinogen concentrate or cryoprecipitate.

Conclusion

Trauma-induced coagulopathy is a complex and dynamic disorder of hemostasis that significantly contributes to mortality and morbidity among severely injured patients. It develops as a consequence of the interaction between tissue injury, hypoperfusion, the inflammatory response, platelet dysfunction, activation of fibrinolysis, and endothelial dysfunction, while its progression is further aggravated by hypothermia, acidosis, and hemodilution. Early recognition of TIC using conventional laboratory testing and viscoelastic methods enables timely identification of specific hemostatic abnormalities and implementation of targeted therapy. Contemporary treatment strategies, including damage control resuscitation, rational use of blood components, correction of hypofibrinogenemia, and early administration of tranexamic acid, contribute to reduced mortality and improved clinical outcomes. Further advances in the understanding of the underlying pathophysiological mechanisms and the development of personalized therapeutic strategies may further improve the management and outcomes of patients with trauma-induced coagulopathy.

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CONVENTIONAL INFECTIOUS SCREENING MARKERS AND EMERGING PATHOGENS IN BLOOD DONOR POPULATION IN ALBANIA

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Abstract

Monitoring transfusion-transmissible infections (TTIs) among blood donors provides essential evidence for improving blood safety and optimizing donor recruitment strategies.

We retrospectively analyzed serological screening data (HBsAg, anti-HCV, HIV Ag/Ab and Syphilis) from 605,027 blood donations collected in Albania between 2004 and 2025 and evaluated NAT (triple test HBV/HCV/HIV), results for 344319 donations following its introduction in 2016, as well as results from newly implemented testing NAT ArboPlex (4000 donations) and NAT UltrioPlex E (1000 donations) during 2025, with Panther System. A detailed analysis of 51,962 donors from Tirana (2024–2025) assessed TTI distribution according to donor type, age, and concordance between serology and NAT. Serology was performed using AxSYM initially and ARCHITECT CMIA since 2008, while NAT triple testing used Procleix Panther and Cobas MPX platforms.

HBsAg prevalence showed a significant decline, from a peak of 6.66% in 2009 to 2.54% in 2025, with a marked reduction after the introduction of vaccinated donor cohorts. No significant long-term changes were observed for HCV, HIV, or syphilis. Young voluntary non-remunerated blood donors (VNRBD) showed the lowest TTI prevalence. NAT-positive/serology-negative donations were exclusively HBV, indicating occult HBV infection. Family/replacement donors and older donors had significantly higher infection rates.

Increasing recruitment and retention of young VNRBD is crucial for improving blood safety, reducing discarded components, and ensuring long-term blood supply sustainability.

Blood Donors; Hepatitis B; emerging pathogens

Background

The prevalence and trends of transfusion-transmissible infections (TTIs) among blood donors are important indicators of blood safety and may reflect infection patterns in the general population. Changes in donor demographics, particularly the increasing contribution of young voluntary non-remunerated blood donors (VNRBD), together with implementation of advanced screening technologies such as nucleic acid testing (NAT), have contributed to improving transfusion safety.

Transfusion-transmissible infections (TTIs) remain a central and evolving threat to blood safety, with hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and syphilis continuing to dominate routine donor screening panels. Although contemporary blood systems have reduced risk through layered safeguards (donor selection, sensitive serology, confirmatory testing, and—where available—molecular screening), residual risk persists because of infectious donations can occur during early infection and because some infections present with low-level or intermittent markers that challenge standard algorithms (1).

This study aimed to evaluate the long-term prevalence and trends of conventional TTIs among Albanian blood donors from 2004 to 2025 and to analyze recent demographic patterns, donor type differences, and concordance between serological and NAT testing in order to support evidence-based donor recruitment and retention strategies. The study evaluated for the first time NAT testing results of emerging pathogens in blood donors in Albania.

Methods

A retrospective analysis was performed using National Blood Transfusion Center registry data. Serological results from 605,027 donations collected between 2004 and 2025 were analyzed for HBsAg, anti-HCV, HIV Ag/Ab, and syphilis markers. In 2004, testing was performed using the AxSYM Abbott platform for viral markers and RPR for syphilis. Since 2008, ARCHITECT CMIA has been used for serological screening, with syphilis confirmation by RPR and TPHA. NAT triplex testing was introduced in 2016 using the Grifols Procleix Panther System, and since 2019 cobas MPX on the cobas 6800 platform has also been implemented. During 2025 NAT testing for Arboviruses and HEV has been added for blood donors from all affected WNV regions in Albania. This testing has been performed in Panther system with NAT ArboPlex (Zika, Chikungunia, WNV, Dengue) (4000 donations) and NAT UltrioPlex E (1000 donations).

A detailed evaluation of 51,962 donations collected in Tirana during 2024–2025 assessed TTI distribution by donor type (family replacement donors and VNRBD), sex, and age groups (<30, 30–45, and >45 years). NAT triple test was applied both to serology-negative donations and for confirmation of repeatedly reactive serological results.

Statistical analysis was performed according to the objective of each comparison. A paired two-sample t-test was used to compare mean annual TTI prevalence rates between the two time periods (2006–2015 and 2016–2025) in order to evaluate long-term temporal changes. The two-proportion Z test was applied to compare TTI prevalence between donor groups (family replacement versus voluntary non-remunerated donors) and among different age categories in the 2024–2025 tirana donor population. Statistical significance was defined as $p < 0.05$.

Results

A significant decline in HBsAg prevalence was observed over the study period, decreasing from the highest value of 6.66% in 2009 to 2.54% in 2025. The average HBsAg prevalence decreased significantly between the periods 2006–2015 and 2016–2025 (5.64% vs. 3.85%). This decline coincides with the increasing presence of donors vaccinated against hepatitis B. Population-level prevention reshapes donor TTI profiles over time. In Albania, universal infant HBV vaccination was introduced in the mid-1990s, and cohort effects are expected to progressively reduce HBV exposure and carriage among younger donors (2). Donor-based evidence from Southern Europe supports the plausibility of such cohort effects, with lower HBV exposure markers in vaccinated or younger groups (3).

No statistically significant differences in mean prevalence between the two decades were observed for HCV, HIV, or syphilis.

Since NAT implementation, 344,319 donations have been tested. HBV NAT yield decreased in the last two years to 1:413 compared with previously reported 1:217, potentially reflecting younger donor demographics as well as improved confirmation algorithms. No NAT yield was observed for HCV or HIV.

No NAT positive donations for Arboviruses and HEV were detected.

Among the 51,962 donors analyzed in 2024–2025, 36,293 (70%) were family/replacement donors and 15,669 (30%) were VNRBD. Overall, 31% of donors were younger than 30 years, 45% were 30–45 years, and 24% were older than 45 years. Among VNRBD, 46% were younger than 30 years and approximately 80% were below 45 years, demonstrating a favourable demographic profile. Previous studies and WHO recommendations have shown that regular voluntary non-remunerated blood donors represent the safest donor population, with lower rates of transfusion-transmissible infections compared with family/replacement donors (4, 5).

Overall serological TTI prevalence was 3.5%, with HBsAg representing the main marker (2.6%). NAT-positive/serology-negative donations accounted for 0.25% of donations and were exclusively HBV infections, consistent with occult hepatitis B infection (OBI). Similar findings have demonstrated that HBV represents the main NAT yield in regions with intermediate HBV endemicity because of occult infection and low-level HBV DNA persistence (6–8).

Infection prevalence was significantly higher among family/replacement donors compared with VNRBD for both serology (4.24% vs. 1.8%) and NAT (0.3% vs. 0.1%). This supports previous evidence that donor type and demographic characteristics are major determinants of residual transfusion risk (4, 5, 9).

Age strongly influenced TTI distribution. Serological prevalence was 0.9%, 4.6%, and 4.7%, while NAT prevalence was 0.01%, 0.17%, and 0.73% in donors aged <30, 30–45, and >45 years, respectively. Lower HBV prevalence among younger donors has been associated with hepatitis B vaccination programs and birth cohort effects. (10, 11)

Overall, 72% of serology-reactive donations were confirmed by NAT. Confirmation rates differed by marker, reaching 91% for HBsAg, but only 25% for anti-HCV and 30% for HIV Ag/Ab. Discordance between serological reactivity and NAT confirmation, particularly for anti-HCV and HIV screening assays, has been reported due to resolved infections, non-specific reactivity, or false-positive screening results (12, 13).

Conclusion

Over two decades, Albania has achieved a significant reduction in hepatitis B prevalence among blood donors, largely associated with the impact of vaccination and changing donor demographics. Young VNRBD represent the safest donor population and are essential for improving both blood safety and sufficiency. Strategies focused on recruiting and retaining young voluntary donors, including encouraging repeated donation, may reduce discarded components and strengthen long-term sustainability. Comprehensive follow-up algorithms, particularly for non-confirmed reactive serology results, remain important to avoid unnecessary donor loss.

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Introduction lecture / Uvodno predavanje UV18

HOW MUCH SAFER IS BLOOD TRANSFUSION TODAY?

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Abstract

Over the past decades, significant progress has been achieved in ensuring the highest possible safety of blood and blood products for transfusion. Careful donor selection, serological screening, and individual-donation nucleic acid testing (ID-NAT PCR) have substantially reduced the risk of transfusion-transmitted infections (TTIs), particularly those caused by HIV, HCV, and HBV. ID-NAT PCR shortens the infectious window period and enables detection of viral genomes before the appearance of serological markers, thereby further enhancing transfusion safety. Nevertheless, residual risk remains due to early-stage infections, low viral loads, viral genetic variability, and limitations in test sensitivity. Hepatitis B virus represents a particular challenge because occult hepatitis B infection (OBI) may remain undetected by standard serological methods; therefore, combined testing for HBsAg, anti-HBc, and HBV DNA is recommended. In addition to established TTIs, increasing attention is being paid to newly identified pathogens, including hepatitis E virus, whereas transfusion transmission of SARS-CoV-2 has not been confirmed. The prevalence of TTIs among blood donors in Serbia is low and continues to decline. Continuous development of diagnostic methods, surveillance of emerging pathogens, and implementation of pathogen inactivation technologies remain essential for further improving viral blood safety.

Keywords: blood transfusion, viruses, blood screening.

Sažetak

Tokom poslednjih nekoliko decenija postignut je značajan napredak u obezbeđivanju maksimalne bezbednosti krvi i hemoprodukata za transfuziju. Brižljiva selekcija davalaca krvi, serološki skrining i pojedinačno testiranje davalaca na nukleinske kiseline (ID NAT-PCR), dovelo je do višestrukog smanjenja rizika od transfuzijski prenosivih infekcija (TPI), posebno infekcija izazvanih virusima HIV, HCV i HBV. ID NAT-PCR omogućava skraćenje "perioda prozora" infekcije i otkrivanje virusnih genoma pre pojave seroloških markera, čime se dodatno povećava bezbednost transfuzije. Ipak, rezidualni rizik i dalje postoji zbog ranih faza infekcije, niskog virusnog opterećenja, genetske varijabilnosti virusa i ograničene osetljivosti pojedinih testova. Poseban izazov predstavlja virus hepatitisa B zbog mogućnosti okultne infekcije (OBI), koja može ostati neotkrivena standardnim serološkim metodama. Zbog toga se preporučuje kombinovano testiranje na HBsAg, anti-HBc i HBV-DNK. Pored klasičnih TPI, raste značaj novootkrivenih patogena, uključujući virus hepatitisa E, dok transfuzijski prenos SARS-CoV-2 nije potvrđen. Prevalenca TPI među davaocima krvi u Srbiji je niska i pokazuje trend daljeg opadanja. Kontinuirani razvoj dijagnostičkih metoda, praćenje novih uzročnika i primena tehnologija inaktivacije patogena predstavljaju ključne strategije za dalje unapređenje virusne bezbednosti krvi i krvnih produkata.

Ključne reči: transfuzija krvi, virusi, skrining krvi

Significant progress has been made in ensuring and maintaining the microbiological safety of units of blood and blood components. Owing to advances in donor screening methods, laboratory testing, and the implementation of modern technologies, the risk of transfusion-transmitted infection associated with a single unit of blood has decreased by three to four orders of magnitude over the past fifty years. Nevertheless, any viral infection may be transmitted through transfusion if an asymptomatic phase of viremia is present in the donor, if the virus is present in the blood at a sufficiently high concentration, if it is capable of surviving the processes of blood collection and blood component storage, and if it can subsequently establish infection in the recipient following intravenous administration.

Careful selection of voluntary blood donors, establishment of regular donor databases, advances in our understanding of

viral biology and epidemiology, and the continuous development of highly sensitive and specific serological and molecular screening methods over the past several decades have resulted in a substantial reduction in the risk of transfusion-transmissible viral infections. Particular progress has been achieved in preventing the transmission of hepatitis C virus (HCV) and human immunodeficiency virus (HIV), with the routine implementation of nucleic acid testing (NAT) reducing the residual risk of transfusion transmission to an almost negligible level. In addition, surveillance of viral genotypic variability is of particular importance for the development and establishment of representative international reference materials, enabling reliable assessment of assay performance, as well as standardization and validation of screening tests.

In contrast, considerably less attention has been devoted to parasitic infections and arthropod-borne infections (vector-borne infections), despite their increasing importance for the safety of transfusion therapy. Although most of these pathogens are rarely transmitted through transfusion, their relative importance is increasing in parallel with the continuous decline in the risk of "classical" transfusion-transmissible viral infections as a result of improvements in screening methods and other blood safety measures.

Despite substantial global progress in improving blood safety, marked differences among countries persist with regard to the risk of transfusion-transmissible viral infections. These differences are determined by the economic and infrastructural capacities of healthcare systems, the local epidemiological situation, the availability of advanced diagnostic technologies, and the level of residual risk considered acceptable by regulatory authorities, transfusion services, and society at large.

The U.S. Food and Drug Administration (FDA) introduced antibody testing for *Treponema pallidum* in the 1950s as the first test aimed at preventing transfusion-transmitted infections (TTIs) (1). During the 1960s, post-transfusion hepatitis (PTH) was found to be strongly associated with transfusion of blood from paid donors, leading to the development of the first test for detection of hepatitis B surface antigen (HBsAg) (2). Testing for antibodies to hepatitis C virus (HCV) was introduced during the 1990s, following the cloning of HCV and its identification as the causative agent of hepatitis C (3). The discovery of human immunodeficiency virus (HIV) as the causative agent of AIDS, followed by the rapid introduction of antibody testing in 1985, resulted in a dramatic reduction in transfusion-transmitted HIV infections, particularly among patients with hemophilia (4). Improvements in serological assays for the detection of antibodies to TTI pathogens, followed by the introduction of HIV-1 p24 antigen testing, HCV antigen testing, and viral nucleic acid testing (NAT-PCR), further reduced the number of transfusion-transmitted viral infections. Today, the risk is so low that it can no longer be assessed through prospective clinical studies and can instead be estimated only by theoretical mathematical models.

The fundamental cause of the residual risk of infection transmission is related to the early phase of infection, when the blood donor is in the so-called "window period" (WP), i.e., the period during which antibodies to TTI pathogens cannot be detected by serological assays. However, because no test is capable of detecting an infectious agent immediately after acquisition of infection, the window-period phenomenon persists. If blood donation occurs during this period, infected blood may enter the blood supply intended for therapeutic use.

With the use of individual-donation nucleic acid testing (ID-NAT-PCR) for the detection of circulating viral nucleic acids, the window period for HIV is 5.6 days, 4.9 days for HCV, and 20 days for HBV (5). The average window period with mini-pool NAT-PCR (MP-NAT-PCR) is 9 days for HIV and 7.4 days for HCV. The window period for detection of HBsAg is at least 30–38 days (6).

A large number of advanced serological assays for the detection of antibodies to TTI pathogens are currently available. Repeat testing using enzyme immunoassays (EIA) and chemiluminescent immunoassays (ChLIA) represents the first step in blood screening and is necessary to identify samples that are likely to be antibody-positive for TTI pathogens. To determine whether a positive result truly indicates infection or represents a false-reactive result, more specific serological confirmatory assays, such as recombinant Western blot or immunoblot assays, are performed. Importantly, every blood unit yielding a repeatedly reactive screening result must be permanently excluded from clinical use, regardless of the results of confirmatory or supplementary testing.

The application of modern technologies has enabled the development of a new generation of serological assays for antibody detection, as well as combined assays capable of simultaneously detecting antigens and antibodies, whose sensitivity approaches that of NAT-PCR methods (7). NAT-PCR involves extraction of nucleic acids from donor plasma, amplification, and detection of specific viral genetic sequences. In developed countries, NAT is used for primary blood donor screening for HBV DNA, HCV RNA, and HIV RNA (8). Although this technology is considered costly, its implementation makes a significant contribution to public health (9). This remains a major challenge in developing countries, where the prevalence of TTIs is higher than in developed countries but where routine NAT-PCR screening cannot be implemented because of its high cost.

NAT-PCR assays must undergo continuous improvement through molecular surveillance of emerging nucleotide sequences, as infectious agents are constantly evolving and modifying their genomes through point mutations and recombination. This issue was highlighted by the inability of some commercially available qualitative NAT-PCR assays to detect rare HIV variants (10), and particularly certain HCV genotypes (11). Interestingly, the problem is even more pronounced with quantitative assays used to determine specific HCV genotypes and HIV RNA copy numbers (12). As a consequence

of using such "inadequate" assays, some TTIs may remain undetected. For example, cases of HBV transmission have been documented in South Africa despite the simultaneous use of serological testing and ID-NAT-PCR screening (13).

Two major factors may affect the reliability of NAT-PCR screening. The first factor influencing NAT-PCR results is the analytical sensitivity of detection in the MP-NAT-PCR approach (mini-pool testing). If the analytical sensitivity of the assay is lower than the number of viral nucleic acid copies present in the sample, a false-negative result may occur. This issue is of particular importance for viruses with a slow replication rate, such as HBV. To overcome this limitation, the use of highly sensitive MP-NAT-PCR assays with the smallest feasible number of samples per pool is recommended, or, alternatively, the use of the more sensitive individual-donation NAT-PCR (ID-NAT-PCR) approach. The second factor affecting NAT-PCR results is the presence of mutations in viral RNA. In HIV infection, viral RNA is reverse-transcribed into DNA through the catalytic activity of reverse transcriptase. Errors occurring during this process cannot be corrected because reverse transcriptase does not possess nucleic acid proofreading or repair activity. Consequently, researchers continuously strive to develop assays based on the amplification and detection of at least two conserved regions of the HIV-1 genome. In the context of the aforementioned limitations in assay reliability, it is important to emphasize that transfusion of more than 5 mL of plasma from an individual with a viral load below 200 copies/mL may result in transmission of HIV infection (14).

Among the TTI pathogens subject to mandatory screening, hepatitis B virus (HBV) represents one of the most complex infectious agents, with its structural characteristics having a substantial impact on testing results. The most effective approach to overcoming diagnostic challenges in HBV infection is triple screening, comprising testing for anti-HBc, HBsAg, and HBV DNA. The presence of circulating HBV DNA in the absence of detectable hepatitis B surface antigen (HBsAg), outside the window period, is characteristic of occult hepatitis B virus infection (OBI). OBI is characterized by a low and fluctuating viral load (≤100 IU/mL), which frequently results in intermittent detection of viral DNA. Most individuals with OBI have detectable anti-HBc antibodies, while approximately 50% are positive for both anti-HBc and anti-HBs antibodies.

A small proportion of individuals with OBI have anti-HBs as the only serological marker, whereas individuals without any detectable serological markers are classified as having "primary OBI" (15). The risk of HBV transmission through blood donated by individuals with OBI ranges from 2% to 48%. Higher viral loads and the absence of anti-HBs antibodies are associated with an increased risk of transmission. In addition, the volume of transfused plasma correlates with the risk of transmission. The infectious dose of HBV, initially estimated at 100 IU, has been revised to approximately 3 IU in more recent studies (16).

The prevalence of TTIs among blood donors in Serbia during the period from 2005 to 2017 was 0.087% for HBV, 0.064% for HCV, 0.013% for HIV, and 0.04% for syphilis, which may be considered very low (17). Although military personnel may have an increased risk of TTIs, the prevalence of these infections among blood donors at the Military Medical Academy in Belgrade was also very low (0.2% for HBV, 0.12% for HCV, 0.005% for HIV, and 0.06% for syphilis) (18). Between 2005 and 2017, a declining trend in the prevalence of HBV and HCV infections was observed, whereas the prevalence of HIV infection and syphilis remained unchanged (17,18). At the Military Medical Academy, the prevalence of HBV in 2025 was 0.03%, while that of HCV was only 0.02%.

Testing for anti-HTLV-I/HTLV-II, *Trypanosoma cruzi*, West Nile virus, and Zika virus is not mandatory but is necessary in areas where these infectious agents are endemic. The first documented case of direct transmission of hepatitis E virus (HEV) from a blood donor to a transfusion recipient was reported in Japan. Since then, numerous cases of transfusion-transmitted hepatitis E (TT-HEV) have been reported worldwide, including in France and the United Kingdom, highlighting the need for broader implementation of HEV screening in transfusion services (19). To date, no confirmed case of SARS-CoV-2 transmission through blood transfusion has been documented (20).

Careful blood donor selection, supported by enhanced donor questionnaires, and laboratory testing represent two key components of the screening process. Testing must be performed accurately and in accordance with the manufacturer's instructions for use. In addition, a system for quarantine storage of potentially positive blood components is essential.

Thanks to modern donor-selection strategies and routine laboratory screening, the residual risk of transfusion-transmitted infection with routinely screened infectious agents has now been reduced to a minimum. Nevertheless, maintaining the level of safety achieved requires continuous epidemiological surveillance for the emergence of new TTIs, as well as the timely implementation of validated methods for their detection.

Pathogen inactivation may in the future provide an additional level of protection against infectious agents for which no screening assays are currently available. The development of pathogen-inactivation technologies will remain an important area of research in transfusion medicine throughout the 21st century. Pathogen inactivation represents an additional defense mechanism developed by humans in the ongoing effort to protect the blood supply against the large number of known and unknown microorganisms capable of compromising blood safety.

Since ensuring the maximum possible safety of blood and blood products is an imperative, the ultimate goal should be the implementation of individual-donation NAT-PCR testing together with serological assays exhibiting the highest possible analytical and clinical sensitivity.

Therefore, continued research and development of diagnostic methods within transfusion services are essential to en-

sure and further enhance the optimal level of safety of blood and blood products.

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TRANSFUSION IN PEDIATRIC PATIENTS: EVIDENCE-BASED GUIDELINES

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Abstract

Evidence-based medicine is the conscientious, reasonable, and clear use of the best currently available evidence in making decisions about the treatment of individual patients. Evidence-based medical practice integrates individual clinical expertise with the best available clinical evidence from systematic research.

Guidelines were developed by integrating global transfusion practices and data from pediatric transfusion research. These guidelines provide direction for transfusion practice in pediatric patients in our country. The World Health Organization's Global status report on blood safety and availability 2025 highlights significant variation in transfusion practices worldwide. Developing evidence-based strategies to improve transfusion protocols and conducting high-quality research are essential. In resource-limited countries, pediatric transfusion challenges include blood supply shortages, the unavailability of blood components, and rising demand. Conversely, high-income countries should aim to prevent unnecessary transfusions. Whenever feasible, blood alternatives and hemostatic agents, such as antifibrinolytics, should be used.

Keywords: Transfusion, pediatrics, guidelines, survey, safe blood

Sažetak

Medicina zasnovana na dokazima je savesna, razumna i jasna upotreba najboljih trenutno dostupnih dokaza u donošenju odluka pri lečenju pojedinačnih pacijenata. Medicinska praksa zasnovane na dokazima predstavlja integrisanje individualne kliničke stručnosti sa najboljim dostupnim kliničkim dokazima iz sistematskih istraživanja.

Kombinovanjem iskustava iz transfuzijske prakse širom sveta, kao i podataka iz studija i istraživanja koja se odnose na transfuzijsku medicinu u dečijoj populaciji, formirani su trenutno važeći vodiči. Iz njih se mogu preuzeti smernice za transfuzijsku praksu kod pedijatrijskih bolesnika u našoj zemlji. Prema globalnom izveštaju o stanju bezbednosti i dostupnosti krvi Svetske zdravstvene organizacije iz 2025. godine, postoje velike varijacije u transfuzijskoj praksi u svetu. Ključan je razvoj strategija za poboljšanje transfuzijske prakse zasnovane na dokazima i visokokvalitetnim istraživanjima. Pedijatrijska transfuzija u zemljama sa ograničenim resursima susreće se sa problemima nedovoljne transfuzije i nedostupnosti komponenti krvi pri povećanim zahtevima, a s druge strane, u zemljama sa visokim nacionalnim dohotkom, pojavljuje se potreba za izbegavanjem transfuzija koje nisu neophodne. Kad god je moguće, neophodno je koristiti alternative za krv i hemostatske agense.

Ključne reči: Transfuzija, pedijatrija, vodiči, anketa, bezbedna krv

Evidence-based medicine includes accurate diagnostic tests, powerful prognostic markers, and effective and safe therapeutic, rehabilitative, and preventive medical interventions. Physicians who practice evidence-based medicine identify and implement the most effective treatment modalities to maximize the quality and length of life of individual patients (1, 2).

Pediatric transfusion practice varies considerably from region to region. For a decade, the most difficult situation has been in sub-Saharan Africa, which includes 49 countries and over a billion inhabitants. A major challenge is caring for children with malaria complicated by intestinal infections, malnutrition, and anemia, which is also the most common cause of hospitalization and mortality. Due to limited resources and cultural differences, blood donation rates are low. Therefore, a hemoglobin (Hgb) level of 40-60 g/l in children is considered moderate anemia, and, according to the World Health Organization (WHO), is not treated with transfusion if there are no clinical symptoms of anemia. The first part of the *Transfusion and Treatment of Severe Anemia in African Children (TRACT)* trial included 1, 565 children from Uganda and Malawi. It led to the recommendation that severe anemia (Hgb less than 40 g/l) be treated with whole blood at 20 ml/kg body mass (BM), due to the safer use of whole blood and the technical challenges of producing blood components (3). The second

randomization within the study included 3196 children with an average age of 37 months. In the group receiving whole blood at 30 ml/kg BM, mortality decreased from 5% to 3% within 28 days of transfusion. In 2021, based on the study results, Point-of-Care Hgb testing was introduced in African hospitals as an essential diagnostic test (4). Another problem in the sub-Saharan region is that 5 million people have sickle cell disease. Strategies applied in the care of these patients include the introduction of a uniform diagnostic test, education of health workers, improved access to health care, and the establishment of centers for specialized care and research for this disease (5).

In 2022, a questionnaire on pediatric transfusion practices was administered to 200 transfusion centers in India, with a 50% response rate. The questionnaire revealed heterogeneity and a lack of standardization. Antibody screening is performed in 57.4% of centers, and O RhD-negative blood is most frequently used in 48.5% of centers (6). A retrospective study of pediatric intensive care units (PICU) at a tertiary care hospital in Western India found inappropriate use of platelet concentrates in 36.9% and fresh frozen plasma (FFP) in 28.9% (7).

In 2017-2018, a retrospective cohort study in China included 5669 newborns. It pointed to the discrepancy between international recommendations and current transfusion practice, including the increased use of erythrocyte transfusions and FFP in newborns. The National Health Commission of the Republic of China approved the 2022 National Guideline for Pediatric Transfusion Practice (8, 9).

For many years, pediatric transfusion practice in Europe has been based on a restrictive strategy for erythrocyte transfusions, as recommended by the international TAXI consensus (Pediatric Critical Care Transfusion and Anemia Expertise Initiative) in 2018 (10). A sudden increase in Hgb levels has been associated with an increased risk of adverse effects of transfusion and worse outcomes in critically ill children. Restrictive transfusion regimens are also applied in the perioperative period in children, according to the guide of the *European Society of Anesthesiology and Intensive Care (ESAIC*), and are supported by the *Transfusion Requirements in Pediatric Intensive Care Unit (TRIPICU) study* (2007), which showed that the restrictive threshold for blood transfusion at Hgb 70 g/L in clinically stable children in the intensive care unit does not lead to increased mortality or multiple organ dysfunction compared with the liberal transfusion regime (11). Perioperative red blood cell transfusion in neonates and infants: *NEonate and Children audiT of Anesthesia pRactice IN Europe (NECTARINE)* is the name of the prospective observational multicenter study from 2016/2017, which included 5, 609 patients from 165 centers in 31 European countries. Real-world practice has shown that transfusion thresholds are often lower than those indicated for infants and children in guidelines. The recommended perioperative Hgb thresholds are 85-120 g/L, depending on the child's age in weeks (12).

During 2023, an electronic web survey was conducted to assess the Hgb threshold for a pediatric patient undergoing erythrocyte transfusion, as part of the so-called TUPAC initiative (*TransfUsion triggers in Pediatric perioperAtive Care*). Pediatric anesthesiologists from university hospitals in the Nordic countries (Denmark, Sweden, Finland, Norway, and Iceland) participated in it. Apart from the initially low Hgb level, the decision to apply erythrocyte transfusion depended, in order of importance, on: lactate level, slowing of heart rate, prolonged capillary filling, drop in blood pressure, decrease in oxygen saturation in the central veins, and decrease in diuresis. A liberal regimen of transfusions was switched to in the event of severe comorbidities and the development of septic shock (13). In 2025, the results of the National Survey: "*How we transfuse children in Italy*" were published. In all 14 hospitals, leukodepleted and irradiated blood components are available, and in 20%, cytomegalovirus-negative; only in some, pathogen-inactivated blood components (13). Evaluation of transfusion practice in neonatology in the USA in 2021 included 7 geographic areas and 60, 243 newborns in a four-year period. There was great variability in decisions to transfuse erythrocytes, RBCs, and platelets, which depended on gestational age and diagnosis. As a rule, all transfusions were administered at higher levels (Hgb 105 g/l, platelet count 45×109/l, and INR 1.7) than recommended by the American Association of Blood Banks (AABB) guideline (14).

The most extensive survey, conducted as an international forum, included 17 pediatric hospitals across five continents. The questions were related to the preparation, selection, safety, and application of small volumes of blood components, i.e., neonatal and pediatric doses. In all centers, units of erythrocytes (aged 3 to 7 days) and ZSP were divided into smaller portions of 40-90 ml. In some centers, there was no time limit for dividing doses (Spain). In Canada, irradiated blood components have a shelf life of only 24 hours. Pathogen-inactivated platelets are prepared in the US and Saudi Arabia, while European countries such as Italy, the UK, and the Netherlands produce solvent-detergent virus-inactivated plasma. Leukoreduced blood components are considered cytomegalovirus (CMV) safe, so CMV testing is performed only on request; in Israel, all blood units are tested for CMV (15).

The transfusion practice of using platelet concentrate (Plt) was monitored for 6 weeks among children aged 3 days to 16 years in 82 PICUs across 16 countries worldwide. The study ran from September 2016 to April 2017. The majority of transfusions were prophylactic 67%, 21% were used to treat minor bleeding, and 12% were Plt transfusions due to extensive bleeding (16). The study investigating the outcomes of administered Plt transfusions within the program, *the Recipient Epidemiology and Donor Evaluation Study-IV-Pediatric (REDS-IV-P)*, was conducted in the USA from 2019 to 2023 across 22 hospitals and 7 blood banks, covering the population from birth to 18 years. Of almost 250, 000 pediatric patients, 3.6% received Plt transfusions. Platelets that were pathogen-reduced, prepared in a platelet additive solution, stored for more than 3 days, and from donors older than 40 years were associated with a lower posttransfusion increment of Plt in patients,

which simultaneously required a higher number of Plt transfusions. The decrease in the effectiveness of Plt transfusions did not affect clinical outcomes; there was no prolongation of hospitalization or increase in mortality. The majority of Plt transfusions were given at a higher pre-transfusion Plt count than recommended: for newborns, 67.8% at a Plt count >25 $\times 10^9$/L, and for older children, 81% at a Plt count >10 $\times 10^9$/L.

The currently valid transfusion guidelines are: *Guidelines on transfusion for fetuses, neonates, and older children* (The British Committee for Standards in Hematology - BCSH, 2016); *Patient Blood Management Guidelines: Module 6, Neonatal and Paediatrics* (National Blood Authority Australia, 2016); *Transfusion Guidelines for Injured Children Using a Modified Delphi Consensus Process* (Collaborators of the Pediatric Emergency Care Applied Research Network - PECARN, 2019); *Consensus Blood Product Transfusion Guidelines for a Large Neonatal Care Network*, USA 2023; and *Red Blood Cell Transfusion 2023 AABB International Guidelines*. Most of these guidelines recommend antifibrinolytics and other strategies to reduce blood loss, as well as intraoperative blood salvage (19, 20).

Conclusion

The transfusion threshold for erythrocyte use is an Hgb level of 70 g/L. At higher Hgb levels, erythrocyte transfusions should be reserved for exceptional cases, based on the patient's age and diagnosis. Except in massive transfusions, FFP is not used for volume replacement. Platelet concentrate transfusions are indicated only during active bleeding, while prophylactic transfusions should be kept to a minimum. Additional evaluation of transfusion practices in children with septic shock, extensive trauma, hematologic-oncology, and transplant patients receiving cellular therapy is needed.

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Introduction lecture / Uvodno predavanje UV20

MANAGEMENT OF POSTPARTUM HEMORRHAGE

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Abstract

Postpartum hemorrhage (PPH) is defined as blood loss greater than 500 mL after vaginal delivery or greater than 1000 mL after a cesarean section within the first 24 hours postpartum. It is a life-threatening medical emergency that requires immediate intervention. The primary causes of PPH are commonly categorized by the "4Ts": tone (uterine atony), tissue (retained placenta), trauma (genital tract lacerations), and thrombin (coagulopathy).

Clinical signs and symptoms include heavy or prolonged bleeding, weakness, tachycardia, dizziness, cold extremities, hypotension, and loss of consciousness. Since visual estimation of blood loss is inaccurate, objective assessment should be performed gravimetrically and through the use of a cell saver. Laboratory diagnosis of PPH includes blood typing (if not previously performed), complete blood count (CBC), and hemostasis testing, including PT, aPTT, fibrinogen (Fib), D-dimer, rotational thromboelastometry (ROTEM), and/or thromboelastography (TEG). Transfusion therapy in PPH is indicated in cases of massive and continuous bleeding. It is discontinued once the bleeding is controlled, target laboratory parameters are achieved, and clinical symptoms resolve. Target parameters include: Hgb > 70 g/L, PLT > 50×10^9/L, and Fib > 1.0 g/L (optimally > 2.0 g/L), along with a normal APTT, INR < 1.3, and the restoration of normo/hypercoagulable profiles on ROTEM. Intraoperative autologous erythrocyte reinfusion (cell salvage) reduces the reliance on allogeneic donor transfusions, helps prevent massive blood transfusion syndrome, significantly improves the postoperative course, and reduces the length of hospital stay.

Successful management of PPH requires a well-organized, emergency response by a multidisciplinary team with clearly defined roles to provide individualized patient care. The combined use of point-of-care (POC) coagulation monitoring, autologous erythrocyte transfusions, coagulation factor concentrates, and synthetic hemostatics reduces the need for allogeneic blood components, making PPH treatment more timely, effective, and safe.

Keywords: postpartum hemorrhage, rotational thromboelastometry, coagulopathy.

Sažetak

Postporođajno krvarenje (PPH) se definiše kao gubitak krvi >500 ml nakon vaginalnog porođaja ili >1000 ml nakon carskog reza u prvih 24 sata. To je životno ugrožavajuće medicinsko stanje koje zahteva hitnu intervenciju. Primarni uzroci PPH se obično kategorišu pomoću akronima „4T": tonus (atonija materice), tkivo (zadržana placenta), trauma (laceracije genitalnog trakta) i trombin (koagulopatija).

Klinička slika i dijagnostika: Klinički znaci i simptomi uključuju obilno ili produženo krvarenje, slabost, tahikardiju, vrtoglavicu, hladne ekstremitete, hipotenziju i gubitak svesti. Pošto je vizuelna procena gubitka krvi netačna, objektivnu procenu treba izvršiti gravimetrijski i upotrebom cell saver-a. Laboratorijska dijagnoza PPH uključuje određivanje krvne grupe (ako nije prethodno urađena), kompletnu krvnu sliku (KKS) i testove hemostaze, uključujući PT, aPTT, fibrinogen (Fib), D-dimer, rotacionu tromboelastometriju (ROTEM) i/ili tromboelastografiju (TEG). Transfuzijska terapija kod PPH je indikovana u slučajevima masivnog i kontinuiranog krvarenja. Prekida se kada je krvarenje pod kontrolom, postignu ciljni laboratorijski parametri i klinički simptomi nestanu. Ciljni parametri uključuju: Hgb > 70 g/L, Plt > 50×109/L i Fibrinogen > 1,0 g/L (optimalno > 2,0 g/L), zajedno sa normalnim APTT-om, INR < 1,3 i obnavljanjem normo/hiperkoagulabilnih profila na ROTEM-u. Intraoperativna autologna reinfuzija eritrocita (spašavanje ćelija) smanjuje oslanjanje na transfuziju alogenih hemoprodukata, pomaže u sprečavanju sindroma masivne transfuzije krvi, značajno poboljšava postoperativni tok i skraćuje dužinu boravka u bolnici.

Uspešno lečenje PPH zahteva dobro organizovanu, hitnu akciju multidisciplinarnog tima sa jasno definisanim ulogama u pružanju individualizovane nege pacijenta. Kombinovana upotreba praćenja koagulacije na mestu nege (POC), autolog-

nih transfuzija eritrocita, koncentrata faktora koagulacije i sintetičkih hemostatika smanjuje potrebu za alogenim komponentama krvi, čineći lečenje PPH blagovremenijim, efikasnijim i bezbednijim.

Ključne reči: postporođajno krvarenje, rotaciona tromboelastometrija, koagulopatija

Introduction

Postpartum hemorrhage (PPH) is any bleeding after delivery involving blood loss greater than 500 mL after vaginal delivery or greater than 1000 mL after cesarean section within the first 24 hours. It is a serious, life-threatening medical condition that requires immediate treatment. Postpartum hemorrhage remains the leading cause of maternal morbidity and mortality in most countries worldwide (1). Blood loss in PPH can occur early (primary PPH), occurring immediately or within the first 24 hours, or late (secondary PPH), occurring from 24 hours up to 6 weeks (42 days) after delivery. Postpartum hemorrhage can also be classified by extent and severity. Massive blood loss is defined as a single loss of ≥ 1500 mL of blood (25–30% of circulating blood volume – CBV) or ≥ 2500 mL of blood (50% of CBV) within 3 hours. In recent diagnostic criteria, instead of the fixed threshold of 500 mL, a new criterion has been proposed: blood loss ≥ 300 mL combined with signs of hemodynamic instability, or ≥ 500 mL regardless of hemodynamic parameters. This reduces the time to diagnosis from 30 to 15 minutes and eliminates underestimation of the amount of blood lost (1, 2).

Etiology

Understanding the etiology of PPH is essential for its prevention and treatment. The underlying causes of PPH are commonly described by the acronym “4T”: tone, tissue, trauma, and thrombin (i.e., poor uterine tone, retained placental tissue, birth trauma, and coagulopathy).

Clinical presentation and diagnosis

Clinical signs and symptoms include heavy or prolonged bleeding, weakness, tachycardia, dizziness, a sensation of cold, a drop in blood pressure, and possible loss of consciousness. Signs of shock may also occur, such as confusion, blurred vision, and clammy, cold skin.

The risk of postpartum hemorrhage (PPH) is increased by complications during pregnancy or by assisted reproductive technology (ART/IVF) procedures. Massive blood loss may lead to severe complications: acute respiratory distress syndrome (ARDS), shock, acute kidney injury (AKI), disseminated intravascular coagulation (DIC), pituitary necrosis (Sheehan syndrome), and loss of fertility (2).

A detailed history and identification of risk factors allow patients to be stratified into low-, intermediate-, and high-risk groups. On gynecological examination of a patient with PPH, the source of bleeding (cervical, uterine, vaginal, perineal, or rectal) should be accurately identified through inspection of the birth canal, vaginal examination, and manual exploration of the uterine cavity. Pulse and blood pressure should also be measured, the lungs auscultated, the abdomen and uterus palpated, the placenta examined, and the amount of blood lost objectively assessed (gravimetrically or using a cell saver). Visual estimation of peripartum blood loss has been shown to be inaccurate, so objective clinical signs and symptoms must be incorporated into the assessment of PPH. Ultrasound examination of the uterus is also helpful in determining the cause of bleeding, allowing assessment of the uterine cavity and detection of free fluid in the abdominal cavity (3).

Laboratory Diagnosis of PPH includes blood typing (if not previously performed), a complete blood count (CBC), and hemostasis testing (PT, aPTT, fibrinogen [Fib], D-dimer), as well as rotational thromboelastometry (ROTEM) and/or thromboelastography (TEG) (4). Coagulopathy may sometimes be the primary cause of pathological blood loss or may develop as a result of massive hemorrhage. Dynamic assessment of the hemostatic system in postpartum women is therefore very important. Rotational thromboelastometry (ROTEM) enables rapid, differentiated identification of hemostatic disorders and is part of point-of-care (POC) diagnostics. This assay uses whole blood, eliminating the need for centrifugation, and hemostasis is assessed directly, taking into account blood temperature and acid–base balance. This method allows rapid assessment of most components of the hemostatic system and guides targeted replacement therapy for deficient coagulation factors. The use of ROTEM significantly reduces unnecessary use of fresh frozen plasma (FFP) and platelet concentrates, while enabling timely, targeted fibrinogen replacement (4, 6).

From the very first minute of bleeding, good organization within a multidisciplinary team (obstetrician, anesthesiologist, transfusion specialist or hematologist, and blood transfusion laboratory staff) with a clear division of responsibilities is essential. The goal is to carry out successful management of PPH that is individualized for each patient and directly dependent on the cause of bleeding. Pharmacotherapy begins with uterotonic agents (oxytocin, carbetocin, misoprostol,

or other prostaglandins), followed by tranexamic acid, infusion of isotonic crystalloid solutions, and uterine massage. If bleeding continues, the obstetrician thoroughly examines the birth canal and manages any visible injuries and lacerations. Blood and blood component replacement is initiated in parallel, and if a disorder of the hemostatic system is detected, hemostatic agents are administered (a repeat dose of tranexamic acid, fibrinogen concentrate or cryoprecipitate, calcium, prothrombin complex concentrate [PCC], and recombinant activated factor VII [rFVIIa]). Bleeding caused by traumatic factors is managed surgically. The World Health Organization (WHO) also recommends the use of a non-pneumatic anti-shock garment (NASG) for managing childbirth outside the hospital, with the aim of stabilizing maternal shock during transport to a healthcare facility. External aortic compression devices may also be used, as well as uterine balloon tamponade methods (such as the Bakri balloon). Balloon tamponade devices may be left in the uterine cavity for up to 24 hours during PPH management (1, 6). Surgical intervention is undertaken if conservative medical management fails or in cases of severe lacerations and uterine rupture. Surgical methods include ligation of the hypogastric, uterine, or ovarian arteries, ligation of the internal iliac artery, placement of compression sutures (B-Lynch), selective embolization of blood vessels, and, as a last resort, hysterectomy (1, 3, 5, 6).

Various professional and healthcare associations currently recommend clear protocols for PPH management to ensure rapid and timely administration of blood components (1, 5, 7).

Transfusion Management in PPH is undertaken in cases of massive and continuous bleeding and is discontinued once bleeding is controlled, target laboratory parameters are reached, and clinical symptoms of shock resolve. Target parameters include: Hgb > 70 g/L, PLT > 50 × 10^9/L, Fib > 1.0 g/L (optimally > 2.0 g/L), a normal aPTT, INR < 1.3, and achievement of a normocoagulable or hypercoagulable status on ROTEM. Administration of tranexamic acid (TXA) effectively reduces the extent of bleeding and the risk of hysterectomy. For blood loss under 1000 mL, it is given at a dose of 15 mg/kg (on average 1 g) intravenously over 10 minutes, with a possible increase to 40 mg/kg (i.e., 4 g) if bleeding continues. The dose may be repeated after 8 hours. A high dose of TXA can reduce the volume of blood loss and the need for donor blood transfusion. Adequate, timely administration of TXA significantly helps reduce mortality, morbidity, and the incidence of hysterectomy in women with massive hemorrhage (1, 8, 9).

When blood loss reaches ≥ 25–30% of CBV and hypocoagulability develops, PCC containing factors II, VII, IX, and X should be administered (1 IU of coagulation factor activity being equivalent to the amount contained in 1 mL of normal human plasma). If no clinical effect is seen within 20 minutes, the same dose is repeated, or fresh frozen plasma (FFP) transfusion is administered (1, 9).

Administration of rFVIIa may be considered in patients with life-threatening hemorrhage only after all conventional measures (including surgical hemostasis and adequate blood component replacement therapy) have failed. Recombinant activated factor VII (rFVIIa) is administered for uncontrolled bleeding at a dose of 90 μg/kg (micrograms per kilogram).

If clinically indicated, the dose may be repeated after 3 hours. Significantly reduced drug efficacy occurs under conditions of hypothermia (below 34°C), acidosis (pH below 7.2), and marked thrombocytopenia (below 50 × 10^9/L) and hypofibrinogenemia (below 0.5 g/L), making it essential to maintain normal homeostasis. The use of rFVIIa should not delay surgical intervention, nor should it be considered a substitute for it (1, 4, 9).

The use of sodium etamsylate and calcium chloride as stand-alone effective hemostatic agents has not been clinically proven. Calcium chloride should primarily be used to correct hypocalcemia or during massive transfusion to prevent citrate intoxication and hyperkalemia (with the use of longer-stored red blood cells). Donor platelet transfusion is indicated when the platelet count falls below 50 × 10^9/L. The initial therapeutic dose consists of 1 apheresis platelet concentrate (or 4 individual concentrates for every 4 units of packed red blood cells) (1, 3).

The use of PCC, rFVIIa, and FFP requires reassessment of hemostatic parameters after 6 hours, as well as administration of a prophylactic dose of low-molecular-weight heparin (LMWH) 6–12 hours after bleeding has been successfully controlled (i.e., after the end of surgery). Prevention of venous thromboembolic complications is necessary in all cases where blood loss exceeded 1000 mL and allogeneic blood component transfusions were administered, provided no active contraindications exist (6, 9). Intraoperative autologous erythrocyte reinfusion (autologous transfusion using a cell saver) significantly reduces the use of donor red blood cells, helps avoid the development of massive transfusion syndrome, substantially improves the postoperative course, and shortens the length of hospital stay. Autologous blood is collected using specially designed devices, by vacuum suction directly from the operative field. The absolute indication for intraoperative cell salvage (ICS) is postpartum hemorrhage, as well as any abdominal delivery in which intraoperative blood loss greater than 20% of CBV is anticipated. Absolute contraindications to ICS are the presence of purulent or fecal content in the abdominal cavity, as well as the presence of substances in the shed blood that are contraindicated for intravenous administration (hydrogen peroxide, distilled water, collagen-based local hemostatics, etc.). When autologous erythrocytes are reinfused in patients with PPH and a history of malignancy, reinfusion must be performed using special leukocyte depletion filters. Theoretical concerns regarding the safety of intraoperative cell salvage in obstetric surgery (risk of amniotic fluid embolism or alloimmunization) have not been confirmed in contemporary clinical practice (1–3, 7–9).

Conclusion

Although PPH is unpredictable and can occur even in pregnant women without any risk factors, adequate antenatal preparation (timely treatment of anemia in pregnancy), prevention of bleeding during delivery, early recognition of symptoms, strict adherence to care algorithms, and rapid availability of medications and blood components can prevent tragic outcomes. Good organization and the combined use of modern POC coagulation and hemostasis monitoring (ROTEM/TEG), together with autologous erythrocyte transfusion, infusion of coagulation factor concentrates, and synthetic hemostatics, drastically reduce the need for transfusion of allogeneic (donor) blood components. This approach makes PPH management more timely, far more effective, and safer for the patient.

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8. KONGRES
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MEDICINE CONGRESS OF SERBIA
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APSTRAKTI / ABSTRACTS

USMENE PREZENTACIJE / ORAL PRESENTATIONS

SAVA CENTAR / SAVA CENTER
Beograd, SRBIJA / Belgrade, Serbia
29–31. oktobar, 2026. / October 29th–31st, 2026

UP 1

DESETOGODIŠNJA RETROSPEKTIVNAANALIZA STRUKTURE DOBROVOLJNIH DAVALACA KRVI (2016–2025): UTICAJ GLOBALNE ZDRAVSTVENE KRIZE NA GENERACIJSKI JAZ

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Uvod: Stabilnost lanca snabdevanja krvlju zavisi od kontinuiranog priliva dobrovoljnih davalaca. Tokom desetogodišnjeg periodog ciklusa (2016–2025), zdravstveni poremećaji i društvene promene transformisali su demografsku strukturu davalaca, uz progresivno starenje redovne baze koja se približava zakonskoj starosnoj granici. **Cilj:** Analiza procentualne distribucije i trendova među tri starosne grupe davalaca od 2016. do 2025. godine: Grupa 1 (18–25), Grupa 2 (26–45) i Grupa 3 (46–65 godina), radi identifikacije segmenta kom je najhitnije potrebna motivaciona intervencija.
Materijal i metode: Retrospektivna studija obuhvatila je podatke iz informacionog sistema (2016–2025) dobijene iz standardizovanih medicinskih upitnika pre donacije. Davaoci su stratifikovani u tri grupe, a analiziran je njihov godišnji udeo u posmatranoj populaciji (G1+G2+G3=100%).
Rezultati: Tokom 10 godina uočava se strukturni poremećaj. Pre pandemije (2016–2019), Grupa 1 je bila stabilna sa prosekom od 29,47% (maksimum 32,96% u 2016). Tokom pandemijskog šoka (2020–2021) zabeležen je oštar pad na minimum od 14,77% (2021) usled zatvaranja obrazovnih ustanova. U post-pandemijskoj fazi (2022–2025), nakon kratkog skoka u 2023. (20,55%), Grupa 1
ponovo opada na 16,71% u 2025. Nasuprot tome, Grupa 3 (46–65) linearno raste sa 22,87% na 31,10%, dok dominantna Grupa 2 ostaje stabilna na oko 52%.
Zaključak: Grupa 1 (mladi) predstavlja najkritičniji segment kom je neophodna hitna intervencija. Strategije regrutacije moraju se preusmeriti ka digitalnom i vršnjačkom angažovanju kroz reklame i društvene mreže kako bi se sprečio kritičan deficit zaliha dok se Grupa 3 približava zakonskoj starosnoj granici.
Ključne reči: dobrovoljno davalaštvo krvi, demografske promene, starosne grupe, zdravstvena kriza, generacijski jaz

UP 1

A TEN-YEAR RETROSPECTIVE ANALYSIS OF VOLUNTARY BLOOD DONOR STRUCTURE (2016–2025): THE IMPACT OF A GLOBAL HEALTH CRISIS ON THE GENERATIONAL GAP

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Introduction: The stability of the blood supply chain relies on a continuous influx of voluntary donors. Over a ten-year period (2016–2025), health disruptions and social shifts transformed the demographic structure of donors, causing a progressive aging of the regular base as they approach the legal age limit.
Objective: To analyze percentage trends among three specific donor age groups from 2016 to 2025: Group 1 (18–25), Group 2 (26–45), and Group 3 (46–65 years), identifying the
segment in most urgent need of intervention.
Material and Methods: A retrospective study extracted data from the information system (2016–2025) using standard pre-donation medical questionnaires. Donors were stratified into three groups, focusing on their annual share within the observed population (G1+G2+G3=100%).
Results: A distinct structural shift occurred over the decade. Pre-pandemic (2016–2019), Group 1 was stable at an average of 29.47% (peaking at32.96% in 2016). The pandemic shock (2020–2021) caused a sharp decline to a historical minimum of 14.77% in 2021 due to school closures. In the post-pandemic phase (2022–2025), despite a brief peak in 2023 (20.55%), Group 1 fell again to 16.71% in 2025. Conversely, Group 3 (46–65) grew linearly from 22.87% to 31.10%, while Group 2 remained stable at around 52%. **Conclusion:** Group 1 represents the most critical segment requiring immediate intervention. Recruitment-strategies must pivot toward digital and peer-to-peer engagement via advertisement and social
media to prevent a critical supply deficit as Group 3 steadily approaches the legal age limit.
Keywords: voluntary blood donation, demographic shifts, age groups, health crisis, generational gap

UP 2

ANALIZA NEŽELJENIH REAKCIJA KOD DOBROVOLJNIH DAVALACA KRVI U INSTITUTU ZA TRANSFUIJU KRVI SRBIJE U PERIODU OD 2021 DO 2025

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Uvod: Dobrovoljno davanje krvi predstavlja bezbedan i rutinski medicinski postupak, ali se kod određenog broja davalaca krvi mogu javiti neželjene reakcije različitog intenziteta, koje se mogu podeliti na blage, srednje teške i teške. Praćenje i analiza neželjenih reakcija vodi ka unapređenju procesa davanja krvi i povećanju bezbednosti davalaca krvi.
Cilj: Cilj rada je analiza učestalosti i strukture neželjenih reakcija kod davalaca koji su krv dali klasičnim putem, u periodu od 2021 do 2025. god u Institutu za transfuziju krvi Srbije.
Metode: Analiza podataka izvršena je retrospektivnim uvidom u bazu podataka iz informacionog sistema Instituta za transfuziju krvi Srbije, i na osnovu Izvestaja o ozbiljnim neželjenim reakcijama kod davaoca (ITKF 793/1). Analizirani su ukupan broj davanja krvi i učestalost neželjenih reakcija u odnosu na stepen težine. U navedenom periodu ukupno je bilo 296236 dobrovoljnih davanja krvi.
Rezultati: Registrovano je 3664 neželjene reakcije, sto predstavlja učestalost od 1,24% u odnosu na ukupan broj davanja krvi. Prema stepenu težine najveći broj prijavljenih neželjenih reakcija pripadao je blagim (vazovagalnim) reakcijama, kojih je evidentirano 3125 (85,3%). Srednje teških reakcija kao što je gubitak svesti zabeležen je kod 532 (14,5%) davalaca krvi, dok je teških (odloženi gubitak svesti) registrovan u 6 (0,2%) slučajeva. U 1 slučaju registrovana je povreda.
Zaključak: Analiza pokazuje da su blage reakcije bile dominantan tip neželjenih reakcija koje se mogu prevenirati odgovarajućom pripremom kao sto je konzumiranje tečnosti pre davanja krvi, razgovor sa davaocem, kao i adekvatna selekcija i odabir davalaca su bitni elementi u prevenciji neželjenih reakcija.
Ključne reči: davalac krvi, neželjene reakcije, prevencija

UP 2

ANALYSIS OF ADVERSE REACTIONS IN VOLUNTARY BLOOD DONORS AT THE BLOOD TRANSFUSION INSTITUTE OF SERBIA DURING THE PERIOD 2021 - 2025

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Introduction: Voluntary blood donation is a safe and routine medical procedure, however, adverse reactions of varying severity may occur in a certain proportion of blood donors. These reactions can be classified as mild, moderate, or severe. Monitoring and analysis of adverse reactions contribute to improving the blood donation process and enhancing donor safety. **Objective:** The aim of this study was to analyze the frequency and distribution of adverse reactions among donors who donated whole blood during the period from 2021 to 2025 at the Blood Transfusion Institute of Serbia. **Methods:** Data were analyzed retrospectively using Institute's information system database and reports on serious donor adverse reactions (ITKF 793/1). The total number of blood donations and the frequency of adverse reactions according to severity grade were evaluated. During the study period, a total of 296,236 voluntary blood donations were recorded. **Results:** A total of 3,664 adverse reactions were reported, corresponding to an a incidence of 1.24% of all donations. According to severity grading, the majority of reported adverse reactions, were mild vasovagal reactions, with 3,125 (85.3%) recorded. Moderate reactions, such as loss of consciousness, were observed in 532 donors (14.5%), while severe reactions (delayed loss of consciousness) were registered in 6 cases(0.2%). One case of donation-related injury was also reported. **Conclusion:** The analysis demonstrated that mild reactions were the predominant type of adverse reactions among blood donors. Many of these reactions can be prevented through appropriate donor prepation, including adequate fluid intake before donation, effective communication with the donors, and careful donor selection. These measures represent important elements in the prevention of adverse reactions and the improvement of donor safety.
Keywords: blood donors, adverse reactions, prevention

UP 3

ANALIZA NAJČEŠĆIH RAZLOGA ZA ODBIJANJE DOBROVOLJNIH DAVALACA KRVI NA TERITORIJI JUGOISTOČNE SRBIJE

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Uvod/Cilj: Kriterijumi za selekciju davalaca i kriterijumi za trajno ili privremeno odlaganje davanja krvi imaju vitalnu ulogu u bezbednosti transfuzije krvi i osmišljeni su da obezbede sigurnost po zdravlje davaoca i primaoca. Dobro je poznata činjenica da odbijanje davalaca krvi ima negativan uticaj na povratak kako prvih tako i redovnih davalaca. Cilj studije je bio da se analizira učestalost odbijanja i razlozi za odbijanje dobrovoljnih davalaca krvi sa naglaskom na privremena odbijanja zbog niskog nivoa hemoglobina (Hb), kako bi se davaoci identifikovali i pravilno savetovali u cilju povećanja njihovog broja.
Metode: Studijom su obuhvaćeni dobrovoljni davaoci krvi od 1. januara do 31. decembra 2023. godine. U studiju su uključena ukupno 2,322 odbijena dobrovoljna davaoca krvi oba pola, starosti između 18 i 65 godina.
Rezultati: Ukupna prevalenca odbijenih davalaca bila je 4,85%. Najčešći razlog za privremeno odlaganje davanja krvi bio je nizak nivo Hb, koji je utvrđen kod 1.002 davaoca krvi (43,15%). Ostali razlozi su uključivali nizak krvni pritisak (265 davalaca, 11,41%), medikamentozna terapija (172 davaoca, 7,41%), nedavno davanje krvi (133 davaoca, 5,73%), visok krvni pritisak (99 davalaca, 4,26%), poremećaj funkcije štitne žlezde (96 davalaca, 4,13%), nedavna hirurška intervencija (81 davalac, 3,49%).
Zaključak: Rezultati ove studije sugerišu da bi se korišćenjem parametara koji preciznije odražavaju status gvožđa uspostavilo bezbednije davanje krvi za davaoce. U cilju zaštite zdravlja davalaca krvi i adekvatnog snabdevanja krvlju treba primeniti odgovarajuće procedure, koje mogu uključivati privremenu suplementaciju gvožđem.
Ključne reči: davaoci krvi, kriterijumi selekcije, uzroci odbijanja, hemoglobin

UP 3

ANALYSIS OF THE MOST COMMON REASONS FOR VOLUNTARY BLOOD DONOR DEFERRAL IN SOUTHEAST SERBIA

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Background/Aim: Criteria for the selection of blood donors (BDs) and criteria for permanent or temporary postponement of blood donation have a vital role in the safety of blood transfusion. It is a well-known fact that the BDs deferral has a negative effect on the return of both first and regular donors. The aim of the study was to analyze the frequency of deferral and the reasons for deferral of voluntary BDs with an emphasis on temporary deferrals due to low Hb levels, in order to identify temporarily deferred donors and advise them properly in order to increase the number of voluntary donors.
Methods: The study included voluntary BDs from January 1 to December 31, 2023. A total of 2,322 rejected voluntary BDs were included in the study. Donors of both sexes, aged between 18 and 65 years, were included.
Results: The overall prevalence of deferred donors was 4.85%. The most common reason for temporary deferral was low hemoglobin (Hb) level, identified in 1,002 blood donors (43.15%). Other reasons included low blood pressure (265 donors, 11.41%), medication use (172 donors, 7.41%), recent blood donation (133 donors, 5.73%), high blood pressure (99 donors, 4.26%), thyroid dysfunction (96 donors, 4.13%), and recent surgical intervention (81 donors, 3.49%).
Conclusion: The results of this study suggest that implementing parameters that more accurately reflect iron status would help ensure donor safety. To protect the health of blood donors (BDs) and maintain an adequate blood supply, appropriate procedures should be applied, which may include temporary iron supplementation.
Keywords: Blood donors, Selection criteria, Deferral causes, Hemoglobin

UP 4

REGIONALNE RAZLIKE U RAZLOZIMA ODBIJANJA DOBROVOLJNIH DAVALACA KRVI U CRNOJ GORI

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Zavod za transfuziju krvi Crne Gore

Uvod Stabilne i sigurne zalihe krvi zavise od dostupnosti dobrovoljnih davalaca. Odbijanje davalaca predstavlja važan dio procesa selekcije kojim se štiti zdravlje i davaoca i primaoca krvi. Međutim, visoka stopa odbijanja smanjuje raspoloživost krvi i može negativno uticati na motivaciju davalaca. Podaci o regionalnim obrascima odbijanja davalaca u Crnoj Gori do sada nijesu sistematski analizirani.
Cilj Cilj rada je analiza i poređenje razloga odbijanja davalaca krvi u tri regionalna organizaciona dijela Zavoda za transfuziju krvi u Crnoj Gori.
Metode Sprovedena je retrospektivna studija koja je obuhvatila sve kandidate odbijene za davanje krvi u periodu 2021–2025. godine u organizacionim djelovima Zavoda za transfuziju krvi Podgorica, Kotor i Berane. Razlozi odbijanja grupisani su u medicinske i bihevioralne kategorije. Primijenjena je deskriptivna statistika za analizu učestalosti i poređenje regionalnih obrazaca.
Rezultati U posmatranom periodu odbijena su ukupno 10.822 kandidata. Najveći broj odbijanja zabilježen je u Podgorici (83,5%), zatim u Kotoru (10,6%) i Beranama (5,8%).
Najčešći ukupni razlozi odbijanja bili su:
• individualna procjena davaoca (32,4%)
• nizak hemoglobin (15,6%)
• hipotenzija (15,5%)
Uočene su izražene regionalne razlike. U Podgorici dominiraju individualna procjena (33,6%) i anemija (17,8%), dok je u Kotoru i Beranama hipotenzija vodeći razlog odbijanja (46,3% i 53,6%). Respiratorne infekcije i rinitis češći su u sjevernom regionu, dok su rizična ponašanja i medicinski faktori izraženiji u centralnom i južnom regionu.
Zaključak Postoje značajne regionalne razlike u razlozima odbijanja davalaca krvi. Većina vodećih uzroka je privremena i potencijalno preventabilna. Regionalno prilagođene edukativne i preventivne strategije mogu doprinijeti smanjenju stope odbijanja i unapređenju stabilnosti zaliha krvi u Crnoj Gori.
Kljucne rijeci Dobrovoljni davaoci krvi,odbijanje davalaca,medicinski iza bihevioralni razlozi,regionalne razlike,selekcija davalaca,zalihe krvi

UP 4

REGIONAL DIFFERENCES IN REASONS FOR DEFERRAL OF VOLUNTARY BLOOD DONORS IN MONTENEGRO

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Background Stable and safe blood supplies depend on the availability of voluntary blood donors. Donor deferral is an important part of the selection process that protects the health of both donors and recipients. However, a high deferral rate reduces blood availability and may negatively affect donor motivation. Data on regional patterns of donor deferral in Montenegro have not been systematically analyzed so far.
Aim The aim of this study was to analyze and compare the reasons for blood donor deferral in three regional organizational units of the Blood Transfusion Institute of Montenegro.
Methods A retrospective study was conducted including all candidates deferred from blood donation between 2021 and 2025 in the organizational units of the Blood Transfusion Institute in Podgorica, Kotor, and Berane. Reasons for deferral were grouped into medical and behavioral categories. Descriptive statistics were used to analyze frequency and compare regional patterns.
Results During the observed period, a total of 10,822 candidates were deferred. The highest number of deferrals was recorded in Podgorica (83.5%), followed by Kotor (10.6%) and Berane (5.8%).
The most common overall reasons for deferral were:
• individual donor assessment (32.4%)
• low hemoglobin (15.6%)
• hypotension (15.5%)
Pronounced regional differences were observed. In Podgorica, individual assessment (33.6%) and anemia (17.8%) predominated, while hypotension was the leading reason for deferral in Kotor and Berane (46.3% and 53.6%). Respiratory infections and rhinitis were more common in the northern region, whereas risk behaviors and medical factors were more pronounced in the central and southern regions.
Conclusion Significant regional differences in the reasons for blood donor deferral exist. Most leading causes are temporary and potentially preventable. Regionally tailored educational and preventive strategies may contribute to reducing deferral rates and improving the stability of blood supplies in Montenegro.
Keywords voluntary blood donors; donor deferral; medical and behavioral reasons; regional differences; donor selection; blood supply

UP 5

ANALIZA PRIVREMENOG ODBIJANJA DOBROVOLJNIH DAVAOCA KRVI NA BROJ DAVANJA KRVI U JEDNOJ GODINI

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Uvod: Dobrovoljno davanje krvi predstavlja jedan od najvažnijih elemenata zdravstvenog sistema. Potencijalni davaoci mogu biti trajno ili privremeno odbijeni iz medicinskih razloga. Privremeno odbijanje davaoca je važna mera očuvanja bezbednosti donirane krvi, ali može imati značajan psihološki uticaj na davaoce. Kod određenih osoba iskustvo odbijanja može dovesti do smanjenja motivacije, odlaganja narednog davanja ili potpunog odustajanja od dobrovoljnog davanja krvi.
Cilj: Ispitivanje povezanosti između privremenog odbijanja DDK i broja davanja krvi tokom jedne godine, i analiza broja DDK koji su nakon isteka privremene zabrane ponovo pristupili dobrovoljnom davanju krvi.
Metode: Retrospektivna analiza potencijalnih DDK koji su se javili u Institut za transfuziju krvi Srbije i na terenske akcije, u periodu od januara 2020. godine do decembra 2025. godine. Podaci su prikupljeni iz informacionog sistema ITKS.
Rezultati: Od 2020. do 2025. godine broj donacija DDK po godinama iznosio je 58.327, 65.535, 71.992, 75.644, 74.894, 73.706. Broj odbijenih DDK za ovaj period po godinama je iznosio 8.879, 9.825, 10.743, 12.088, 9.467, 10.273. Nakon isteka perioda privremene zabrane tokom iste godine sa doniranjem je nastavilo 24,45%, 22,69% 22,54%, 23,25%, 24,48% i 25,11% DDK.
Zaključak: Posle isteka privremene zabrane samo mali broj DDK krvi se vraća davanju krvi (22-25%). Da bi se problem prevazišao potrebna je kontinuirana edukacija DDK o mogućim razlozima, kao i detaljno objašnjenja DDK koji je privremeno odbijen, uz naglašavanje potrebe da nastavi sa doniranjem krvi nakon isteka privremene zabrane.
Ključne reči: davalac krvi, privremene kontraindikacije, edukacija.

UP 5

ANALYSIS OF THE IMPACT OF TEMPORARY DEFFERAL OF VOLONTARY BLOOD DONORS ON THE NUMBER OF BLOOD DONATIONS IN A YEAR

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Introduction: Voluntary blood donation is one of the most important components of the healthcare system. Potential donors may be permanently or temporarily deferred for medical reasons. Temporary donor deferral is an important measure for maintaining the safety of donated blood; however, it may have a significant psychological impact on donors. For some individuals, the experience of deferral may lead to reduced motivation, postponement of future donations, or complete withdrawal from voluntary blood donation.
Objective: To investigate the association between temporary deferral of voluntary blood donors and the number of blood donations within one year, and to analyze the proportion of donors who returned to donate blood after the expiration of the temporary deferral period.
Methods: A retrospective analysis was conducted on potential voluntary blood donors who presented to the Blood Transfusion Institute of Serbia and at mobile blood donation drives between January 2020 and December 2025. Data were collected from the Institute's information system.
Results: From 2020 to 2025, the annual numbers of blood donations were 58,327; 65,535; 71,992; 75,644; 74,894; and 73,706. The annual numbers of temporarily deferred donors during the same period were 8,879; 9,825; 10,743; 12,088; 9,467; and 10,273. Following the expiration of the temporary deferral period, the proportions of donors who resumed donating blood within the same year were 24.45%, 22.69%, 22.54%, 23.25%, 24.48%, and 25.11%.
Conclusion: After the expiration of a temporary deferral, only a small number of blood donors return to donate blood (22–25%). To address this issue, continuous education of blood donors about possible reasons for deferral is necessary, as well as providing detailed explanations to donors who have been temporarily deferred, emphasizing the importance of resuming blood donation once the temporary deferral period has ended.
Keywords: blood donor, temporary deferral, education.

UP 6

UTICAJ POLNIH RAZLIKA NA UČESTALOST KONTRAINDIKACIJA KOD DAVALACA KRVI

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Uvod: Dostupnost krvi predstavlja ključan faktor za funkcionisanje zdravstvenog sistema. Da bi transfuzija bila bezbedna, neophodna je adekvatna selekcija davalaca. Kako biološke razlike između muškaraca i žena utiču na učestalost bolesti u opštoj populaciji, tako utiču i na kontraindikacije kod davalaca krvi.
Cilj: Utvrditi i uporediti najčešće kontraindikacije kod muških i ženskih davalaca krvi u 2025. godini i definisati mogućnosti smanjenja broja odbijenih davalaca.
Materijal i metode: Retrospektivna studija sprovedena u Institutu za transfuziju krvi Srbije. Analizirani su podaci svih potencijalnih davalaca cele krvi prijavljenih u naš informacioni sistem tokom 2025.godine.
Rezultati: Ukupan broj prijavljenih davalaca iznosio je 84393 (78,1% muškaraca i 21,9% žene). Žene su odbijane više nego dvostruko češće. Kod njih je nizak hemoglobin bio najučestaliji razlog odbijanja (52,8%). Detaljnija analiza prema starosnoj dobi, pokazala je da je procenat odbijenih žena, zbog niskog hemoglobina, najviši u najmlađoj starosnoj grupi (18-24 godine), 14,2%, a najniži u najstarijoj (50-65 godina) - 6,7%. Od odbijenih muških davalaca krvi, njih 28,2% je odbijeno zbog ove kontraindikacije. Hiruške intervencije i poremećaji srčanog ritma su češći razlozi odbijanja muškaraca. Trajne kontraindikacije su retke. Kod muškaraca su dominirale psorijaza i astma, a kod žena hipo i hipertireoza sa trajnom supstitucionom terapijom.
Zaključak: Nizak hemoglobin je glavna kontraindikacija kod žena. Svaka druga odbijena žena, odbijena je zbog ovog razloga. U populaciji muškaraca, kontraindikacije su heterogenije. Kod njih su veće hiruške intervencije i poremećaji srčanog ritma češći, nego kod žena. Posebnu pažnju je neophodno posvetiti sideropenijskoj anemiji kao potencijalno reverzibilnom, ograničavajućem faktoru, kod žena u reproduktivnom periodu.
Ključne reči: davalaštvo krvi; pol; kontraindikacije; sideropenijska anemija

UP 6

IMPACT OF SEX DIFFERENCES ON THE FREQUENCY OF CONTRAINDICATIONS AMONG BLOOD DONORS

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Introduction: Appropriate donor selection is essential for transfusion safety. Biological differences between men and women influence the prevalence of diseases in the general population and may also affect the frequency of contraindications among blood donors.
Objective: To compare the most common contraindications among male and female blood donors in 2025 and identify opportunities to reduce donor deferrals.
Materials and Methods: A retrospective study analyzed data from all prospective whole-blood donors registered in the Blood Transfusion Institute of Serbia information system during 2025.
Results: 84,393 prospective donors were registered; 78.1% were men and 21.9% were women. Women were deferred more than twice as often as men. Low hemoglobin was the leading cause of deferral among women, accounting for 52.8% of female deferrals. Age-stratified analysis showed female low-hemoglobin deferrals peaked in the youngest age group (18–24 years) at 14.2% and were lowest in the oldest age group (50–65 years) at 6.7%. The same contraindication caused 28.2% of male deferrals. Surgical procedures and cardiac arrhythmias were more frequent causes of deferral among men. Permanent contraindications were uncommon. Among men, psoriasis and asthma were the most frequent permanent contraindications, whereas among women, hypothyroidism and hyperthyroidism requiring lifelong replacement therapy predominated.
Conclusion: Low hemoglobin is the leading contraindication among female blood donors, accounting for every second deferral. In men, contraindications were more heterogeneous, with surgical procedures and cardiac arrhythmias occurring more frequently than in women. Special attention should be paid to sideropenic anemia, a potentially reversible factor among women of reproductive age.
Keywords: blood donation; gender; contraindications; sideropenic anemia

UP 7

UVOĐENJE SKRININGA FERITINA KOD DOBROVOLJNIH DAVALACA KRVI – FAZA I

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Uvod Očuvanje zdravlja dobrovoljnih davalaca krvi jedan je od osnovnih ciljeva savremene transfuzijske medicine. U skladu sa preporukama Saveta Evrope o praćenju statusa gvožđa kod davalaca krvi i principima *Donor Blood Management*, Institut za transfuziju krvi Srbije uveo je program skrininga feritina. Cilj prve faze istraživanja bio je utvrđivanje bazalnih vrednosti feritina i učestalosti smanjenih rezervi gvožđa kod osoba koje prvi put pristupaju davanju krvi.
Materijal i metode:U istraživanje su uključena 103 dobrovoljna davaoca krvi koji su prvi put pristupili davanju krvi (72 muškarca i 31 žena). Koncentracija hemoglobina određivana je iz kapilarne, a feritina iz venske krvi. Analizirani su demografski i laboratorijski podaci.
Rezultati: Prosečna starost ispitanika iznosila je 34,4 godine.
Prosečna koncentracija hemoglobina je bila 152,2 g/L (126-179), a feritina 101,3 μg/L (7-304).
Kod žena prosečna koncentracija hemoglobina iznosila je 139,7 g/L (126–156), a feritina 35,9 μg/L (7-145).
Snižene vrednosti feritina (<30 μg/L) utvrđene su kod 20 ispitanika (19,4%), uključujući 17 od 31 žene (54,8%) i 3 od 72 muškarca (4,2%). Vrednosti feritina <15 μg/L registrovane su kod 8 ispitanika (7,8%) uključujući sedam žena i jednog muškarca.
Kod većine ispitanika sa sniženim vrednostima feritina koncentracija hemoglobina bila je u granicama za davanje krvi.
Zaključak Smanjene rezerve gvožđa mogu biti prisutne već kod osoba koje prvi put daju krv. Skrining feritina omogućava potpuniju procenu statusa gvožđa od određivanja hemoglobina. Dobijeni rezultati predstavljaju osnovu za longitudinalno praćenje promena vrednosti feritina nakon ponovljenih davanja krvi i razvoj strategija zasnovanih na dokazima radi očuvanja rezervi gvožđa, unapređenja bezbednosti davalaca i održivosti dobrovoljnog davalaštva krvi.
Ključne reči: dobrovoljno davalaštvo krvi, feritin, rezerve gvožđa, dobrovoljni davaoci krvi.

UP 7

IMPLEMENTATION OF FERRITIN SCREENING IN VOLUNTARY BLOOD DONORS: PHASE I

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Introduction Preserving the health of voluntary blood donors is one of the primary goals of modern transfusion medicine. In accordance with the Council of Europe recommendations on monitoring iron status in blood donors and the principles of donor blood management, the Blood Transfusion Institute of Serbia introduced a ferritin screening program. The aim of the first phase of the study was to determine baseline ferritin levels and the prevalence of reduced iron stores in first-time blood donors.
Materials and Methods The study included 103 first-time voluntary blood donors (72 men and 31 women). Hemoglobin concentration was determined from capillary blood samples, while ferritin concentration was measured in venous blood samples. Demographic and laboratory data were analyzed.
Results The mean age of the participants was 34.4 years. The mean hemoglobin concentration was 152.2 g/L (126–179), and the mean ferritin concentration was 101.3 μg/L (7–304). Among women, the mean hemoglobin concentration was 139.7 g/L (126–156), while the mean ferritin concentration was 35.9 μg/L (7–145). Reduced ferritin levels (<30 μg/L) were detected in 20 participants (19.4%), including 17 of 31 women (54.8%) and 3 of 72 men (4.2%). Ferritin levels <15 μg/L were recorded in 8 participants (7.8%), including seven women and one man. In most participants with reduced ferritin levels, hemoglobin concentrations remained within the eligibility criteria for blood donation.
Conclusion Reduced iron stores may already be present in individuals donating blood for the first time. Ferritin screening provides a more comprehensive assessment of iron status than hemoglobin testing alone. The findings provide a basis for longitudinal monitoring of ferritin levels following repeated blood donations and for the development of evidence-based strategies aimed at preserving iron stores, improving donor safety, and ensuring the sustainability of voluntary blood donation.
Keywords: voluntary blood donation; blood donors, ferritin; iron stores.

UP 8

ULOGA DRUŠTVENO ODGOVORNOG PARTNERSTVA U PROMOCIJI DOBROVOLJNOG DAVALAŠTVA KRVI

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Uvod: Sezonske nestašice krvi predstavljaju kontinuirani izazov za održavanje stabilnog sistema dobrovoljnog davalaštva krvi. Razvoj partnerstava između Crvenog krsta Srbije i društveno odgovornih kompanija otvara mogućnosti za unapređenje promocije dobrovoljnog davalaštva krvi, jačanje angažovanja mladih i organizovanje akcija na lokacijama dostupnim velikom broju građana.
Ciljevi: Analiza efekata dugoročne saradnje sa društveno odgovornom kompanijom na unapređenje programa dobrovoljnog davalaštva krvi, kroz veće uključivanje mladih, podizanje svesti o značaju davalaštva i organizaciju dostupnijih akcija tokom letnjeg perioda radi obezbeđivanja stabilnijih rezervi krvi.
Metode: Analiza trogodišnje saradnje kompanije Lidl Srbija i Crvenog krsta Srbije u oblasti dobrovoljnog davalaštva krvi, kroz podršku Klubovima 25 i organizaciju akcija davanja krvi u Lidl prodavnicama.
Rezultati: Tokom tri godine prikupljeno je 924 jedinice krvi na 52 vanredne akcije u periodu između juna i septembra kada je i najveći izazov doći do davalaca krvi.
5 novih klubova 25 je osnovano sa ciljem motivacije mladih da postanu davaoci krvi i pozovu svoje bližnje da daju krv.
Kroz kampanje na društvenim mrežama podignuta je vidljivost teme dobrovoljnog davalaštva krvi sa ciljem privlačenja mladih davalaca koji do sada nisu dali krv ili su postali pasivni davaoci pa su se aktivirali ponovo. Kroz donaciju robe dodeljeni su mali znakovi pažnje tokom nedelje Crvenog krsta i letnje kampanje uz pomoć kojih su davaoci osetili dodatan osećaj zahvalnosti za njihov dar.
Zaključak: Sprovedena analiza potvrđuje značaj strateškog partnerstva između Crvenog krsta Srbije i društveno odgovorne kompanije u jačanju aktivnosti usmerenih ka promociji dobrovoljnog davalaštva krvi. Kombinacija edukacije i aktivnog uključivanja mladih kroz program Klub 25, zajedno sa organizovanjem akcija na pristupačnim lokacijama, predstavlja održiv model podrške sistemu obezbeđivanja dovoljnih rezervi krvi.
Ključne reči: saradnja, motivacija, Crveni krst

UP 8

THE ROLE OF SOCIALLY RESPONSIBLE PARTNERSHIP IN THE PROMOTION OF VOLUNTARY BLOOD DONATION

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Introduction: Seasonal blood shortages are a continuous challenge for maintaining a stable voluntary blood donation system. The development of partnerships between the Red Cross of Serbia and socially responsible companies opens up opportunities for improving the promotion of voluntary blood donation, strengthening the engagement of young people and organizing blood drives at locations accessible to a large number of citizens.
Objective: Analysis of the effects of long-term cooperation with a socially responsible company on the improvement of the voluntary blood donation program, through greater involvement of young people, raising awareness of the importance of donation and the organization of more accessible blood drives during the summer period in order to ensure more stable blood reserves.
Methods: Analysis of the three-year cooperation between the company Lidl Serbia and the Red Cross of Serbia in the field of voluntary blood donation, through the support of Clubs 25 and the organization of blood drives in the parking lot of Lidl stores.
Results: During three years, 924 units of blood were collected at 52 additional blood drives in the period between June and September, when the greatest challenge is to reach blood donors. 5 new clubs 25 were founded with the aim of motivating young people to become blood donors and invite their relatives to donate blood. Through campaigns on social networks, the visibility of the topic of voluntary blood donation was raised with the aim of attracting young donors who have not given blood so far or who became passive donors and became active again. Through the donation of goods, small tokens of appreciation were given during the Red Cross week and summer campaign, with the help of which donors felt an additional sense of gratitude for their good deed.
Conclusion: The conducted analysis confirms the importance of the strategic partnership between the Red Cross of Serbia and a socially responsible company in strengthening activities aimed at the promotion of voluntary blood donation. The combination of education and active involvement of young people through the Club 25 program, together with the organization of blood drives in accessible locations, represents a sustainable model of support for the system of providing sufficient blood reserves.
Keywords: cooperation, motivation, Red Cross

UP 9

BLOOD DONOR SATISFACTION -INDICATOR OF THE QUALITY OF THE BLOOD COLLECTION PROCESS AT THE SLOVENIAN INSTITUTE FOR TRANFUSION MEDICINE

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For an efficient blood supply in Slovenia, which is based on non-remunerated blood donation, a sufficient number of blood donors is of key importance, especially their willingness to donate blood regularly. Numerous factors in the blood collection process can affect the experience and satisfaction of the blood donor, and thus their decision to return. In accordance with the ISO 9001 quality standard, which, requires regular monitoring of service user satisfaction and continuous improvement of processes, we conduct blood donor satisfaction measurements at the Slovenian Institute for Transfusion Medicine.
The purpose of the research is to assess the impact of changes in the blood collection process in recent years on blood donor satisfaction.
The objectives are: to determine the level of blood donor satisfaction with individual elements of the blood collection process, to analyze the impact of factors such as the attitude and professionalism of the staff, the organization of the process and the comfort of the procedure on blood donor satisfaction,to determine the connection between blood donor satisfaction and their willingness to donate blood again, to identify key factors that significantly affect blood donor satisfaction, to propose improving the quality of services and the experience of blood donors.
Methods: The research is based on a survey of blood donors in Slovenia over a period of 1-3 months, using a structured questionnaire that includes demographic data, assessment of individual phases of the blood donation process, staff attitude, organization, and overall satisfaction and behavioral intentions of blood donors.
Results: The results of the analysis of blood donor satisfaction measurements of approximately 2,500 blood donors will be presented, with an assessment of the importance of the influence of factors of the individual blood collection process on blood donor satisfaction.
Conclusion: Blood donation is a voluntary act, therefore ensuring high quality services, a friendly attitude, and professional treatment is of key importance for maintaining blood donor satisfaction and long-term willingness to cooperate.

Key words: blood donor, satifaction, quality system

UP 9

BLOOD DONOR SATISFACTION – ASSESMENT OF THE PROCESS QUALITY AT THE SLOVENIAN INSTITUTE FOR TRANFUSION MEDICINE

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Introduction: A sufficient number of blood donors, particularly their willingness to donate blood regularly, is essential for maintaining an adequate blood supply in Slovenia, where the blood supply system is based on voluntary, non-remunerated blood donation. Numerous factors throughout the blood donation process can affect donors' experience and satisfaction and, consequently, their decision to return. In accordance with the ISO 9001 quality standard, the Slovenian Institute of Transfusion Medicine regularly conducts blood donor satisfaction surveys.
Objectives: The objectives were to assess blood donor satisfaction with individual aspects of the blood donation process, identify key factors that significantly influence donor satisfaction, and propose measures to improve the quality of services and the overall donor experience.
Methods: The study was conducted with questionnaire among blood donors in Slovenia from June to September 2026. The questionnaire included basic data, assessment of stages of the blood donation process, staff attitude and communication, organization of the process, as well as overall satisfaction and donors' behavioral intentions.
Results: Preliminary results of a satisfaction survey involving approximately 400 blood donors are presented, including an assessment of the importance of individual factors in the blood donation process and their impact on overall donor satisfaction. In addition results of the analysis of compliments and complaints are presented.
Conclusion: Blood donation is a voluntary act; therefore, ensuring high-quality services, a friendly and respectful approach, and professional conduct by staff are essential for maintaining donor satisfaction and their long-term willingness to return and donate blood.

Key words: blood donor, satifaction, quality system

UP 10

POZITIVAN DIREKTAN ANTIGLOBULINSKI TEST KOD JEDINICA ERITROCITA U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE

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Uvod: Direktan antiglobulinski test (DAT) ili Coombs-ov test nije deo rutinskog testiranja dobrovoljnih davalaca krvi, ali se jedinice eritrocita sa pozitivnim DAT-om otkrivaju u sklopu pretransfuzijskih ispitivanja.
Cilj: Prikaz urađenih DAT analiza kod davalaca krvi u Institutu za transfuziju krvi Srbije. **Materijal i metode:** Retrospektivna analiza DAT rezultata u periodu od 01.01.2024. do 30.04.2026. godine, izvršena je uvidom u protokole Odeljenja, prijave neusaglašenosti/reklamacije jedinica eritrocita i uvidom u informacioni sistem ITKS. DAT se obavlja na automatizovanoj platformi i manuelnom metodom u gelu.
Rezultati: U posmatranom periodu u ITKS-u donirano je 179199 jedinica krvi. Urađene su 564 DAT analize (0,31%). Od ukupnog broja urađenih DAT analiza 130 (23%) je urađeno u sklopu rešavanja reklamacija/neusaglašenosti. Na odeljenje za ispitivanje i kontrolu krvi davalaca prispelo je 130 reklamacija i neusaglašenosti na proizvod, od čega je kod 16 reklamacija DAT bio negativan (12,3%), a kod 114 reklamacija (87,7%) DAT bio pozitivan. Kod 83 jedinice eritrocita (72,8%) potvrđeno je prisustvo antitela klase IgG. U posmatranom periodu urađeno je 19 ponovljenih DAT testiranja kod dobrovoljnih davalaca krvi nakon više od 6 meseci od donacije sa pozitivnim DAT-om. Kod 6 davalaca (36,8%) DAT je bio pozitivan.
Zaključak: Kod 63,2% kontrolnih uzoraka dobijen je negativan rezultat DAT-a, što ukazuje na mogućnost razmatranja ponovnog uključivanja davaoca u davalaštvo krvi.

Ključne reči: DAT, testiranje, eritrociti

UP 10

POSITIVE DIRECT ANTIGLOBULIN TEST IN RED BLOOD CELL UNITS AT THE BLOOD TRANSFUSION INSTITUTE OF SERBIA

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Introduction: Direct antiglobulin test (DAT), also known as the Coombs test, is not part of the routine testing of voluntary blood donors. However, red blood cell units with a positive DAT may be identified during pretransfusion testing.
Aim: To present the results of DAT analyses performed in blood donors at the Blood Transfusion Institute of Serbia.
Materials and Methods: A retrospective analysis of DAT results obtained between January 1, 2024 and April 30, 2026 was conducted through the review of departmental records, reports of product discrepancies and complaints, and the Institute's information system. DAT was performed using both an automated platform and a manual gel card method.
Results: During the study period, 179,199 blood units were donated at the Blood Transfusion Institute of Serbia. A total of 564 DAT analyses, 130 (23%) were carried out as part of investigations of product discrepancies and complaints. A total of 130 complaints and discrepancies related to blood products were received by the Department for Blood Donor Testing; among these, DAT was negative in 16 cases (12.3%) and positive in 114 cases (87,7%). The presence of IgG antibodies was confirmed in 83 red blood cell units (72,8%). During the observed period, 19 repeat DAT test were performed in voluntary blood donors more than six months after donation with a previously positive DAT result. DAT remained positive in 6 donors (36.8%).
Conclusion: In 63.2% of the control samples, a negative DAT result was obtained, indicating the possibility of considering the donor for re-entry into the blood donation program.

Key words: DAT, testing, erythrocytes

UP 11

KOMPARATIVNA ANALIZA FUNKCIONALNOG I STANDARDNOG LABORATORIJSKOG ODREĐIVANJA FIBRINOGENA U KRIOPRECIPITATU

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Uvod: Krioprecipitat predstavlja važnu terapijsku krvnu komponentu bogatu fibrinogenom sa značajnom ulogom u terapiji stečenog i urođenog deficita fibrinogena, naročito u stanjima masivnog krvarenja. Koncentracija fibrinogena se rutinski određuje Clauss metodom, dok FIBTEM test u okviru ROTEM tromboelastometrije omogućava procenu funkcionalnog doprinosa fibrinogena formiranju i stabilnosti fibrinskog ugruška. Podaci o primeni viskoelastičnih metoda u proceni kvaliteta krioprecipitata su ograničeni.
Cilj: Cilj rada bio je ispitivanje povezanosti između koncentracije fibrinogena određene Clauss metodom i funkcionalne procene fibrinogena dobijene FIBTEM testom u jedinicama krioprecipitata.
Materijal i metode: Analizirano je 50 jedinica krioprecipitata. Koncentracija fibrinogena određivana je Clauss koagulometrijskom metodom, dok je funkcionalna procena fibrinogena vršena primenom FIBTEM testa u okviru ROTEM tromboelastometrije. Statistička analiza obuhvatila je procenu korelacije između ispitivanih parametara.
Rezultati: Srednja koncentracija fibrinogena određena Clauss metodom iznosila je 7,48 ± 0,82 g/L, dok je srednja vrednost fibrinogena procenjena FIBTEM testom iznosila 9,44 ± 2,13 g/L. Utvrđena je statistički značajna pozitivna korelacija između ispitivanih metoda ($r = 0,715$; $p < 0,001$), što ukazuje na snažnu povezanost između laboratorijski određene koncentracije fibrinogena i njegovog funkcionalnog doprinosa jačini fibrinskog ugruška. Dobijeni nalazi ukazuju da FIBTEM može predstavljati koristan alat u proceni kvaliteta krioprecipitata i funkcionalne dostupnosti fibrinogena.
Zaključak: FIBTEM test pokazuje dobru povezanost sa standardnim određivanjem fibrinogena Clauss metodom i može doprineti funkcionalnoj proceni kvaliteta krioprecipitata. Primena viskoelastičnih metoda otvara mogućnost savremenijeg pristupa evaluaciji krvnih komponenti i potencijalno bolje procene njihove hemostatske efikasnosti.
Ključne reči: krioprecipitat, fibrinogen, Clauss metoda, tromboelastometrija, viskoelastični testovi

UP 11

COMPARATIVE ANALYSIS OF FUNCTIONAL AND STANDARD LABORATORY FIBRINOGEN ASSESSMENT IN CRYOPRECIPITATES

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Introduction: Cryoprecipitate is an important therapeutic blood component rich in fibrinogen, with a significant role in the treatment of acquired and congenital fibrinogen deficiency, particularly in conditions of massive bleeding. Fibrinogen concentration is routinely determined using the Clauss method, while the FIBTEM test within ROTEM thromboelastometry enables assessment of the functional contribution of fibrinogen to fibrin clot formation and stability. Data regarding the application of viscoelastic methods in the evaluation of cryoprecipitate quality remain limited.
Aim: The aim of this study was to evaluate the association between fibrinogen concentration determined by the Clauss method and functional fibrinogen assessment obtained using the FIBTEM test in cryoprecipitate units.
Materials and Methods: A total of 50 cryoprecipitate units were analyzed. Fibrinogen concentration was determined using the Clauss coagulometric method, while functional fibrinogen assessment was performed using the FIBTEM test within ROTEM thromboelastometry. Statistical analysis included correlation assessment between the investigated parameters.
Results: The mean fibrinogen concentration determined by the Clauss method was 7.48 ± 0.82 g/L, whereas the mean fibrinogen value estimated by the FIBTEM test was 9.44 ± 2.13 g/L. A statistically significant positive correlation was observed between the investigated methods ($r = 0.715$; $p < 0.001$), indicating a strong association between laboratory-determined fibrinogen concentration and its functional contribution to fibrin clot strength. These findings suggest that FIBTEM may represent a useful tool for assessing cryoprecipitate quality and functional fibrinogen availability.
Conclusion: The FIBTEM test demonstrates good agreement with standard fibrinogen determination by the Clauss method and may contribute to the functional assessment of cryoprecipitate quality. The application of viscoelastic methods offers the possibility of a more advanced approach to the evaluation of transfusion products and potentially improved assessment of their hemostatic efficacy.
Keywords: cryoprecipitate, fibrinogen, Clauss method, thromboelastometry, viscoelastic testing

UP 12

PROIZVODNJA, KONTROLA I DISTRIBUCIJA KRIOPRECIPITATA U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE

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Uvod: Na Odeljenju za pripremu komponenata krvi Instituta za transfuziju krvi Srbije (ITKS) krioprecipitat se proizvodi kontrolisano, uz propisane zahteve za kvalitet, a distribucija se vrši ovlašćenim transfuzijskim ustanovama i bolničkim bankama krvi na osnovu trebovanja.
Cilj: Prikazati podatke o proizvedenoj količini, kontroli kvaliteta i distribuciji krioprecipitata u ITKS-u za period od 28 meseci.
Materijal i metode: Retrospektivna analiza podataka iz informacionog sistema ITKS-a o proizvedenoj količini i distribuciji krioprecipitata i rezultata redovne dvomesečne kontrole kvaliteta za period 1.1.2024–18.5.2026.
Rezultati: U ispitanom periodu ukupno je proizvedeno 70.479 doza krioprecipitata (30.480 u 2024, 29.892 u 2025. i 10.107 do 18.05.2026). U odnosu na krvne grupe, najzastupljenija je krvna grupa A (28.443; 40,4%), za njom slede O (25.709; 36,5%), B (11.660; 16,5%) i AB (4.667; 6,6%), pri česmu su Rh-pozitivne jedinice bile zastupljene sa 84%. Od ukupne proizvodnje krioprecipitata distribuirano je 68.066 doza, sa gotovo istovetnom raspodelom krvnih grupa: A (28.227; 41,5%), O (24.058; 35,3%), B (11.282; 16,6%) i AB (4.499; 6,6%). Rezultati kontrole 84 jedinice iz 14 izveštaja su pokazali da je faktor VIIIc bio >70 IJ/jed. u 92,9% jedinica, fibrinogen >140 mg/jed. u 100%, von Vilebrandov faktor >100 IJ/jed. u 98,8%, a medijane su višestruko nadmašile minimume kvaliteta (faktor VIIIc ≈1,7 puta, fibrinogen ≈4,5 puta).
Zaključak: Redovne kontrole su pokazale da je kvalitet krioprecipitata visok i stabilan, što potvrđuje pouzdanost proizvodnog procesa. Krioprecipitat zadržava značajno mesto u terapiji kada je indikovan, a buduće aktivnosti bi bilo dobro usmeriti ka optimizaciji indikacija, unapređenju dostupnosti hemostatske terapije i racionalizaciji upotrebe komponenti krvi.
Ključne reči: krioprecipitat, kvalitet, proizvodnja i distribucija

UP12

PRODUCTION, QUALITY CONTROL AND DISTRIBUTION OF CRYOPRECIPITATE AT THE BLOOD TRANSFUSION INSTITUTE OF SERBIA

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Introduction: At the Department for Preparation of Blood Components of the Blood Transfusion Institute of Serbia (BTIS), cryoprecipitate is produced under controlled conditions and in accordance with defined quality requirements and distributed to authorised transfusion institutions and hospital blood banks upon request.
Aim: To present data on the quantity produced, quality control and distribution of cryoprecipitate at the BTIS over a 28-month period.
Materials and Methods: A retrospective analysis was performed using data from the BTIS information system on cryoprecipitate production and distribution, as well as the results of regular bimonthly quality control, for the period from 1 January 2024 to 18 May 2026.
Results: During the study period, a total of 70,479 units of cryoprecipitate were produced: 30,480 in 2024, 29,892 in 2025, and 10,107 by 18 May 2026. Regarding blood group distribution, group A was the most common (28,443; 40.4%), followed by group O (25,709; 36.5%), group B (11,660; 16.5%) and group AB (4,667; 6.6%), while Rh-positive units accounted for 84% of all units. Of the total cryoprecipitate production, 68,066 units were distributed, with an almost identical blood group distribution: A (28,227; 41.5%), O (24,058; 35.3%), B (11,282; 16.6%) and AB (4,499; 6.6%). Quality control results for 84 units from 14 reports showed that factor VIII:C was >70 IU/unit in 92.9% of units, fibrinogen was >140 mg/unit in 100%, and von Willebrand factor was >100 IU/unit in 98.8%. Median values exceeded the minimum quality requirements several-fold, approximately 1.7-fold for factor VIII:C and 4.5-fold for fibrinogen.
Conclusion: Regular quality control demonstrated that cryoprecipitate quality was high and stable, confirming the reliability of the production process. Cryoprecipitate continues to have an important role in therapy when clinically indicated. Future activities should be directed towards optimising indications, improving the availability of haemostatic therapy and rationalising the use of blood components.
Keywords: cryoprecipitate, quality, production and distribution

UP 13

VISIBLE AGGREGATES IN AMICUS FRESENIUS APHERESIS PLATELET CONCENTRATES

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Introduction: Apheresis platelet concentrates are essential blood components, but visible platelet aggregates may occur during or after collection and affect quality control, product availability and release.
Objective: To determine the frequency and storage behaviour of visible aggregates in Amicus Fresenius apheresis platelet concentrates.
Materials and methods: We retrospectively reviewed 71 Amicus Fresenius plateletpheresis procedures performed during the observed period. All donors were male and met standard eligibility criteria. Platelets were stored in 35% plasma and 65% PAS under continuous agitation and assessed by visual inspection and quality control during five-day storage. For aggregate-positive units, donor and procedure parameters, ABO/RhD group, swirling and aggregate persistence were recorded. Data were analysed descriptively.
Results: Visible aggregates were observed in 11/71 products (15.5%), mostly medium-sized, with large aggregates in some AB-group products. In 10/11 affected products (90.9%), aggregates resuspended between storage days 2 and 3. One product (1/71; 1.4%) had persistent aggregates until expiry with impaired swirling and was discarded. Aggregate-positive donors had median age 38 years, pre-donation platelet count 247×109/L, MPV 9.8 fL and BMI 27.4 kg/m2; 9/11 had BMI ≥25 kg/m2. Median procedure duration was 49 minutes, product volume 289 mL and ACD volume 285 mL.
Conclusion: Initial visible aggregates occurred in 15.5% of products, whereas persistent aggregates were uncommon. Most aggregates resolved during storage with preserved swirling. Systematic inspection during storage remains essential for distinguishing transient aggregates from products requiring discard.
Key words: apheresis platelets; platelet aggregates; Amicus Fresenius; PAS; quality control.

UP 13

UP 14

KAPI ZA OČI OD AUTOLOGNOG SERUMA: OSMOGODIŠNJE ISKUSTVO KBC-A OSIJEK

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Uvod: Kapi za oči od autolognog seruma primenjuju se u lečenju težih bolesti površine oka, prema indikaciji oftalmologa. Njihova proizvodnja u KBC-u Osijek započela je 2017. godine.
Cilj: Prikazati osmogodišnje iskustvo KBC-a Osijek, obim i uspešnost proizvodnje, trendove i najčešće indikacije.
Materijal i metode: Retrospektivno su analizirani podaci o bolesnicima i proizvodnji od jula 2017. do juna 2025. godine: demografski podaci, broj postupaka i proizvedenih setova, uspešnost proizvodnje, trajanje terapije i dijagnoze. Za pripremu 20% rastvora autolognog seruma u fiziološkom rastvoru uzimano je 150 mL krvi bez antikoagulansa.
Rezultati: Obrađeno je 265 bolesnika, među kojima je bilo 226 žena (85 %), a medijana starosti iznosila je 66 godina. Do 31. decembra 2024. sprovedena su 1.234 postupka i proizvedeno 3.546 setova, uz uspešnost proizvodnje od 96 %. Broj postupaka porastao je sa 58 u 2017. na 215 u 2024. godini, a broj setova sa 173 na 611. Terapiju je najmanje tri godine koristilo 52 bolesnika (19,6 %). Najčešće indikacije bile su Sjögrenov sindrom (24,5 %), akutni konjunktivitis (16,6 %) i keratokonjunktivitis (15,8 %). Zbog medicinskih kontraindikacija ili neuspešne proizvodnje pri prvom dolasku, 28 bolesnika (10,5 %) nije započelo ili nastavilo terapiju.
Zaključak: Proizvodnja kapi za oči od autolognog seruma u KBC-u Osijek pouzdana je i uspešna, uz značajan porast obima rada. Omogućava dostupnost dugotrajne terapije bolesnicima iz istočne Hrvatske. Alogene serumske kapi ostaju mogućnost za bolesnike koji nisu kandidati za autolognu proizvodnju.
Ključne reči: autologni serum; kapi za oči; bolesti površine oka; transfuzijska medicina

UP 14

AUTOLOGOUS SERUM EYE DROPS: EIGHT YEARS OF EXPERIENCE AT UNIVERSITY HOSPITAL CENTRE OSIJEK

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Introduction: Autologous serum eye drops are used to treat severe ocular surface diseases when indicated by an ophthalmologist. Their production at University Hospital Centre Osijek began in 2017.
Objective: To present the eight-year experience of University Hospital Centre Osijek, including production volume and success rate, trends, and the most common indications.
Materials and Methods: Patient and production data from July 2017 to June 2025 were retrospectively analysed, including demographic characteristics, the number of procedures and sets produced, production success rate, treatment duration, and diagnoses. To prepare a 20% solution of autologous serum in physiological saline, 150 mL of blood was collected without anticoagulant.
Results: A total of 265 patients were included, 226 of whom were women (85%), and the median age was 66 years. By 31 December 2024, 1,234 procedures had been performed and 3,546 sets produced, with a production success rate of 96%. The number of procedures increased from 58 in 2017 to 215 in 2024, while the number of sets increased from 173 to 611. Fifty-two patients (19.6%) received treatment for at least three years. The most common indications were Sjögren syndrome (24.5%), acute conjunctivitis (16.6%), and keratoconjunctivitis (15.8%). Due to medical contraindications or a failed production attempt at the initial visit, 28 patients (10.5%) did not initiate or continue treatment.
Conclusion: The production of autologous serum eye drops at University Hospital Centre Osijek is reliable and successful, with a substantial increase in production volume. It provides access to long-term treatment for patients from eastern Croatia. Allogeneic serum eye drops remain an option for patients who are not eligible for autologous production.
Keywords: autologous serum; eye drops; ocular surface diseases; transfusion medicine

UP 15

IMPLEMENTACIJA NACIONALNOG PROGRAMA AFEREZNOG PRIKUPLJANJA, KRIOPREZERVACIJE I SKLADIŠTENJA MATIČNIH ĆELIJA HEMATOPOEZE U CRNOJ GORI

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Uvod: Prva procedura afereznog prikupljanja matičnih ćelija hematopoeze (MĆH) u Crnoj Gori izvedena je 23.01.2025. u Zavodu za transfuziju krvi Crne Gore. Program je uspostavljen nakon regulisanja pravnog okvira, adaptacije prostora, nabavke opreme, edukacije kadra i izrade SOP-ova, sa ciljem izvođenja autologni transplantacija u Kliničkom centru Crne Gore, gde je 17.02.2025. izvedena prva autologna transplantacija MĆH u Crnoj Gori.
Cilj: Prikazati program afereznog prikupljanja, krioprezervacije i skladištenja MĆH u Crnoj Gori i prve rezultate iz 2025. godine.
Materijal i metode: Urađena je retrospektivna deskriptivna analiza prve godine primene programa. Analizirani su demografski podaci, mobilizacioni režimi, broj afereznih procedura, doza CD34+ ćelija i postupci krioprezervacije i skladištenja produkata.
Rezultati: U program je uključeno 17 pacijenata, prosečne starosti 57,7 godina. Izvedeno je 26 afereznih procedura, prosečno 1,53 po pacijentu. Najčešća indikacija bila je multipli mijelom (76,5%), a zatim non-Hodgkin limfom (23,5%). Mobilizacija je sprovođena G-CSF kod 41,2% pacijenata, G-CSF + pleriksafor kod 35,3%, hemoterapijom + G-CSF kod 17,6% i hemoterapijom + G-CSF + pleriksaforom kod 5,9%. **Doza CD34+ ćelija po proceduri iznosila je 0,60–10,50 ×10⁶/kg telesne mase, kumulativna doza po pacijentu 2,50–10,50 ×10⁶/kg telesne mase.** Krioprezervacija i skladištenje produkata sprovođeni su prema SOP-ovima.
Zaključak: Rezultati potvrđuju da je Crna Gora uspostavila funkcionalan i održiv model za autolognu transplantaciju MĆH, čime su stvoreni uslovi za lečenje pacijenata u zemlji, uz značajne razvojne i ekonomske koristi za zdravstveni sistem.
Ključne reči: afereza, autologna transplantacija matičnih ćelija hematopoeze, krioprezervacija

UP 15

IMPLEMENTATION OF THE NATIONAL PROGRAM FOR APHERESIS COLLECTION, CRYOPRESERVATION AND STORAGE OF HEMATOPOIETIC STEM CELLS IN MONTENEGRO

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Introduction: The first apheresis collection of peripheral blood hematopoietic stem cells (HSC) in Montenegro was performed on 23 January 2025 at the Institute for Blood Transfusion of Montenegro. The program was established after legal regulation, facility adaptation, equipment procurement, staff training, and SOP implementation, to enable autologous transplantation at the Clinical Center of Montenegro, where the first autologous HSC transplantation in the country was performed on 17 February 2025.
Aim: To present the national program for apheresis collection, cryopreservation and storage of HSC in Montenegro and its first results in 2025.
Methods: Retrospective descriptive analysis of the first program year. Demographic characteristics, mobilization regimens, procedure number, CD34+ cell dose, cryopreservation and storage procedures were analyzed.
Results: Seventeen patients were included, with a mean age of 57.7 years. **Twenty-six apheresis procedures were performed (mean 1.53 per patient).** The most common indication was multiple myeloma (76.5%), followed by non-Hodgkin lymphoma (23.5%). Mobilization was performed with G-CSF in 41.2% of patients, G-CSF plus plerixafor in 35.3%, chemotherapy plus G-CSF in 17.6%, and chemotherapy plus G-CSF plus plerixafor in 5.9%. CD34+ cell dose per procedure ranged from 0.60 to 10.50 ×10⁶/kg body weight, and cumulative dose per patient from 2.50 to 10.50 ×10⁶/kg body weight. Cryopreservation and storage were performed according to SOPs.
Conclusion: Montenegro established a sustainable model for autologous transplantation, enabling treatment in-country and providing economic and developmental benefits.
Keywords: apheresis, autologous HSC transplantation, cryopreservation

UP 16

KOMPARACIJA ADAMII CD34 BROJAČA SA DVE PROTOČNE CITOMETRIJE PRI ODREĐIVANJU BROJA CD34+ MATIČNIH ĆELIJA HEMATOPOEZE

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Uvod: Precizno merenje broja CD34+ ćelija je neophodno za obezbeđivanje adekvatne doze matičnih ćelija hematopoeze (MĆH) za transplantaciju u perifernoj krvi pacijenta pre afereze i u afereznom produktu.
Metode: Kvantifikovali smo CD34+ ćelije koristeći ADAMII CD34+ brojač (NanoEntek, Južna Koreja) u 14/11 uzoraka periferne krvi i 22/17 afereznih produkata dobijenih od MĆH donora radi poređenja sa Navios EX/DxFlex, Beckman Coulter Flow Cytometry platformama, SAD. Poređenje između svake od dve metode obavljeno je korišćenjem Spirmanove ili Pirsonove korelacione analize ($p<0,05$).
Rezultati: Sprovedena je Spirmanova korelaciona analiza ($p<0,05$), koja pokazuje statistički značajnu, umereno jaku, pozitivnu korelaciju između procenta ukupnih CD34+ ćelija merenih pomoću ADAMII i procenta ukupnih CD34+ ćelija u perifernoj krvi ($\rho=0,676$, $p=0,008$), i statistički značajnu, jaku, pozitivnu korelaciju između procenta ukupnih CD34+ ćelija u afereznom proizvodu u poređenju sa Navios EX ($\rho=0,973$, $p=0,000$). Sprovedena je Spirmanova korelaciona analiza ($p<0,01$) koja pokazuje statistički značajnu, jaku, pozitivnu korelaciju između procenta održivih CD34+ ćelija merenih pomoću ADAMII i procenta održivih CD34+ ćelija u perifernoj krvi ($\rho=0,91$, $p=0,000$), i statistički značajnu, jaku, pozitivnu Pirsonovu korelaciju između procenta održivih CD34+ u afereznom proizvodu u poređenju sa BC DxFlex ($\rho=0,978$, $p=0,000$).
Zaključak: ADAMII CD34+ brojač se može koristiti za pouzdanu i brzu kvantifikaciju CD34+ ćelija, omogućavajući tačno određivanje broja CD34+ ćelija u uzorcima periferne krvi i afereznim produktima.

UP 16

COMPARATIVE EVALUATION OF ADAMII IMAGE CYTOMETRY WITH TWO FLOW CYTOMETRY PLATFORMS FOR CD34⁺ HEMATOPOIETIC STEM CELL ENUMERATION

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Background: Precise measurement of CD34+ cells is essential for ensuring an adequate hematopoietic stem cell (HSC) dose for transplantation from apheresis product, and from peripheral blood before apheresis.
Methods: We quantified CD34+ cells using the ADAMII image cytometer (NanoEntek, South Korea) in 14/11 peripheral blood samples and 22/17 apheresis products obtained from HSCT donors for comparison with Navios EX/DxFlex, Beckman Coulter, USA. The comparison between the two methods was performed using Spearman or Pearson correlation analysis ($p<0.05$).
Results: Spearman's correlation analysis was performed, demonstrating a statistically significant, moderately strong, positive correlation between the percentage of total CD34+ cells measured by ADAMII and the percentage of total CD34+ cells in peripheral blood ($\rho=0.676$, $p=0.008$), and a statistically significant, strong, positive correlation between the percentage of total CD34+ cells in the apheresis product when compared with Navios EX ($\rho=0.973$, $p=0.000$). Spearman's correlation analysis was performed, showing statistically significant, strong, positive correlation between the percentage of viable CD34+ cells measured by ADAMII and the percentage of viable CD34+ cells in peripheral blood ($\rho=0.91$, $p=0.000$), and a statistically significant, strong, positive Pearson's correlation between the percentage of viable CD34 in the apheresis product when compared with BC DxFlex ($\rho=0.978$, $p=0.000$).
Conclusion: The ADAMII image cytometry platform can be reliably employed for point-of-care quantification of CD34+ cells in peripheral blood and apheresis products.

UP 17

EKSTRAKORPORALNA FOTOFEREZA - OSNOVNE KARAKTERISTIKE I NAŠA ISKUSTVA

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Uvod: Ekstrakorporalna fotofereza (*engl*. Extracorporeal photopheresis, ECP) je imunomodulatorna terapija, koja se najčešće koristi u lečenju akutne i hronične forme bolesti kalem protiv domaćina (*engl*. Graft versus host disease, GvHD), kutanog T ćelijskog limfoma (*engl*. cutaneus T-cell lymphoma, CTCL), sklerodermije, psorijaze, nakon transplantacije solidnih organa, atopijskog dermatitisa, reumatoidnog artritisa, dijabetesa tip 1 i drugih autoimunih bolesti.
Procedura obuhvata ozračivanje (ultravioletnim zracima) prikupljenih T-limfocita bolesnika, što će dovesti dovesti imuni sistem u ravnotežu reorganizacijom imunološkog odgovora,. Pre zračenja, prikupljenim ćelijama se dodaje 8-MOP (8 metoksipsoralenom), a potom infunduju pacijentu.
Cilj rada: prikazati osnovne karakteristike fotofereze, analizirati savremenu literaturu i iskustva svetskih centara, uz osvrt na sopstvene rezultate tokom trogodišnje primene ECP.
Rezultati: Ukupno je lečeno 18 bolesnika, zbog GvHD (14) kao komplikacije nakon transplantacije kod akutnih leukemija, a četiri bolesnika zbog CTCL. Procesiran je jedan volumen krvi po sesiji (bez prikupljanja plazme), dve sesije nedeljno (GvHD), odnosno dve sesije svake druge nedelje (CTLC), u trajanju od najmanje šest meseci. ECP se pokazala kao neinvazivna, bezbedna i efikasna procedura, sa minimalnim neželjenim dejstvima. ECP smanjuje potrebu za imunosupresivnim lekovima kao i primenu drugih terapija. Značajno je smanjen stepen mortaliteta i morbiditeta i povećan stepen ukupnog preživljavanja. Kod većine pacijenata postignuto je kliničko poboljšanje i dobra kontrola bolesti. Prikazani su slučajevi akutnog GvHD i Sezarijevog sindroma, kod kojih su efekti ECP bili najbolji.
Zaključak: ECP je dokazana efikasna i bezbedna procedura koja ima jasne indikacije, a u bliskoj budućnosti će se one proširiti i na druge bolesti.
Кључне речи: екстракорпорална фотофереза, имуномодулација, Т-лимфоцити, алогена трансплантација, GvHD, CTCL.

UP 17

EXTRACORPOREAL PHOTOPHERESIS - BASIC CHARACTERISTICS AND OUR EXPERIENCE

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Introduction: Extracorporeal photopheresis (ECP) is an immunomodulatory therapy, which is most often used in the treatment of acute and chronic forms of graft versus host disease (GvHD), cutaneous T-cell lymphoma (CTCL), scleroderma, psoriasis, after solid organ transplantation, atopic dermatitis, rheumatoid arthritis, type 1 diabetes and other autoimmune diseases.
The procedure includes irradiation (ultraviolet rays) of collected T-lymphocytes of the patient, which will bring the immune system into balance by reorganizing the immune response. Before irradiation, 8-MOP (8 methoxypsoralen) is added to the collected cells, and then they are infused into the patient.
Aim: to present the basic characteristics of photopheresis, analyze contemporary literature and experiences of world centers, with a review of own results during three years of ECP application.
Results: A total of 18 patients were treated, due to GvHD (14) as complications after transplantation in acute leukemias, and four patients due to CTCL. One volume of blood was processed per session (without plasma collection), two sessions per week (GvHD), or two sessions every other week (CTLC), lasting at least six months. ECP has been shown to be a non-invasive, safe and effective procedure, with minimal side effects. ECP reduces the need for immunosuppressive drugs as well as the use of other therapies. The degree of mortality and morbidity has been significantly reduced and the degree of overall survival has increased. Clinical improvement and good disease control were achieved in most patients. Cases of acute GvHD and Sézary syndrome were presented, in which the effects of ECP were the best.
Conclusion: ECP is a proven effective and safe procedure that has clear indications, and in the near future these will be extended to other diseases.
Keywords: extracorporeal photopheresis, immunomodulation, T lymphocytes, allogeneic transplantation, GvHD, CTCL.

UP 18

IZMENA ERITROCITA KOD DREPANOCITOZE: EFIKASNOST I BEZBEDNOST SISTEMA SPECTRA OPTIA

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Uvod: drepanocitoza (engl. *sickle cell disease*) predstavlja naslednu hemoglobinopatiju koja se karakteriše hroničnom hemolitičkom anemijom, epizodama vazookluzije i oštećenjem različitih organa. Efikasna procedura u prevenciji i lečenju komplikacija bolesti je parcijalna ili potpuna izmena eritrocita, kojom se smanjuje udeo eritrocita koji sadrže haemoglobin S (HbS).
Cilj rada: izneti iskustvo u izmeni eritrocita na "*Spectra Optiji"* kod sedam bolesnika sa drepanocitozom, kao i procenu efikasnosti i bezbednosti procedure.
Materijal i metode: sedam pacijenata sa drepanocitozom, je lečeno od 29. Sept. do 10. Okt 2025. godine u "Etablissement français du sang Nouvelle Aquitaine u Bordou, izmenom eritrocita na aparatu *Spectra Optia* (Terumo BCT). Praćene su indikacije, volumen izmenjene krvi, postignuti nivo HbS nakon procedure i neželjene reakcije.
Rezultati: kod sedam bolesnika je ukupno urađeno sedam procedura. Srednji postignuti FCR (procenat eritrocita koji preostaju nakon procedure) je iznosio nakon izmene 45,4% u odnosu na početni procenat. Cilj je da se izmeni polovina pacijentovih eritrocita, odnosno da FCR bude niži od 50%. Prosečno je aplikovano šest jedinica filtrovanih eritrocita. Od sedam pacijenata, samo je jedna bila žena, uzrasta od 19-46 godina. Pre primene eritrocita radi se unakrsni test, kao i obavezni "bed-side" test, a krv se primenjuje zagrejana. Kod svih pacijenata postignuto je kliničko poboljšanje uz značajno smanjenje učestalosti kriznih epizoda. Nisu zabeležene ozbiljne neželjene reakcije tokom izvođenja procedura.
Zaključak: izmena eritrocita se pokazala kao efikasna i bezbedna metoda u lečenju bolesnika sa drepanocitozom. Pravovremena i pravilno indikovana primena ove procedure doprinosi smanjenju komplikacija bolesti i poboljšanju kvaliteta života pacijenata.

UP 18

RED BLOOD CELL EXCHANGE IN SICKLE CELL DISEASE: EFFICACY AND SAFETY OF THE SPECTRA OPTIA SYSTEM

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Introduction: Sickle cell disease (SCD) is an inherited hemoglobinopathy characterized by chronic hemolytic anemia, vaso-occlusive crises, and progressive organ damage. Red blood cell exchange (RBCX) is an effective treatment that reduces the proportion of erythrocytes containing hemoglobin S (HbS), thereby preventing and treating disease-related complications.
Aim: To present our experience with RBCX performed on the Spectra Optia system in seven patients with SCD and to evaluate its efficacy and safety.
Materials and Methods: Seven patients with SCD underwent RBCX between September 29 and October 10, 2025, at the Etablissement Français du Sang Nouvelle-Aquitaine, Bordeaux, France, using the Spectra Optia apheresis system (Terumo BCT). Indications, exchanged blood volume, post-procedural HbS levels, and adverse reactions were analyzed.
Results: Seven procedures were performed in seven patients. The mean post-procedural Fraction of Cells Remaining (FCR) was 45.4%, achieving the target FCR of <50%. On average, six units of leukocyte-reduced red blood cells were transfused per procedure. Patients were 19–46 years old, and one was female. Crossmatching and bedside testing were performed before transfusion, and all blood products were warmed before administration. Clinical improvement and a reduced frequency of vaso-occlusive crises were observed in all patients. No serious adverse reactions occurred.
Conclusion: RBCX is a safe and effective treatment for patients with SCD. Timely and appropriate use of this procedure reduces disease-related complications and improves quality of life.
Keywords: apheresis, sickle cell disease, red blood cell exchange.

UP 19

DONORSKE TROMBOCITAFEREZE U ZAVODU ZA TRANSFUZIJU KRVI NIŠ ZA PETOGODIŠNJI PERIOD 2020 DO 2024

Milan Petrović
Zavod za transfuziju krvi Niš

UVOD Donorske trombocitafereze su standardna procedura u našoj ustanovi već više od tri decenije.Procedura se sastoji od odvajanja trombocita od unapred pripremljenog davaoca i reinfuzija ostatka krvi nazad. Period između dve donacije ne bi trebo biti kraći od 15 dana.
CILJ Svrha ovog apstrakta je da pokaže kretanje porasta broja hematoonkoloških pacijenata kroz broj procedura,broj napravljenih doza i upoređenje pedijatrijskih i odraslih primaoca afereznih trombocita
MATERIJAL I METODE Mi izvodimo donorske trombocitafereze pomoću Hemonetics MCS+ćelijskog separatora.Kandidati se testiraju (krvna grupa,koagulacija,krvna slika i marker transmisivnih bolesti)I na osnovu rezultata lekar odredjuje ko će biti prihvaćen
REZULTATI u 2020 godini smo imali 65 separacija za 10 odraslih i 55 pedijatrijskih primaoca,50 su bile jedinstvene doze,15 podeljene u dve jednake doze.U 2021godini smo imali 22 separacije,8 za odrasle i 14 za pedijatrijske pacijente.20 su bile cele a 2 su podeljene u dve jednake doze.U 2022 godini smo imali 83 separacije,56 za odrasle i 31 za pedijatrijske primaoce.77 jedinačnih I 6 su bile podeljene u dve jednake doze.U 2023 godini smo imali 166 separacija,142 za odrasle i 24 za pedijatrijske primaoce.146 su bile jedinačne,14 su bile podeljene u dve a 6 podeljene u tri jednake doze.U 2024 godini smo imali 104 separacije,85 za odrasle i 19 za pedijatrijske primaoce.89 su bile jedinačne a 15 su podeljene u dve jednake doze
ZAKLJUČAK Tokom Kovid perioda 2020 i 2021 godine imali smo ograničeni broj raspoloživih davaoca pa smo se usresredili na ranjivije primaoce(pedijatrijske).Kako se situacija menjala broj donora i procedura je rastao tako da je broj procedura za odrasle primaoce nadmašio pedijatrijske

UP 19

PLATELETPHERESIS IN BLOOD TRANSFUSION CENTER NIS IN FIVE YEAR PERIOD 2020 TO 2024

Milan Petrovic
Blood transfusion Institute Nis

INTRO Donor plateletpheresis are standard procedure in our facility for more than three decades.Procedure consists of separating platetets from advance prepared donor and reinfusing rest of the blood back.Period between two donations shouldn't be shorter than 15 days
AIM Point of tis apstract is to show increasing number of hematooncological patients through number of procedures,number of prepared doses and pediatric and adult apheresis platelet recipients comparision
MATERIAL AND METHODS We perform donor plateletpheresis with Hemonetics MCS+ cell separator.Candidates are tested(blood group,-coagulation,blood formula and blood transmissive disease markers)and doctor confirm acceptance considering results.
RESULTS In year 2020 we had 65 separations 10 for adult and 55 for pediatric recipients.50 were single doses,15 divided in two equal doses. In year 2021 we had 22 separations,8 for adult and 14 for pediatric recipients,20 were single and 2 were divided in two equal doses.In year 2022 we had 83 separations,56 for adult and 31 for pediatric recipients.77 were single and 6 were divided into two equal doses.In year 2023 we had 166 separations,142 for adult and 24 for pediatric recipients.146 were single,14 were double and 6 were divided in three equal doses.In year 2024 we had 104 separations,85 for adult and 19 for pediatric recipients.89 were single and 15 were divided in two equal doses
CONCLUSION During Covid period in years 2020 and 2021,we have limited number of donors focusing on more vulnerable recipients(pediatric).As situation changes,number of separations for adult overtake pediatric

UP 20

RETKA, ALI HITNA: TROMBOTSKA TROMBOCITOPENIJSKA PURPURA KROZ PRIKAZ SLUČAJA

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Uvod: Trombotička trombocitopenična purpura (TTP) je veoma retka i po život opasna trombotička mikroangiopatija koju karakterišu mikroangiopatska hemolitička anemija, teška trombocitopenija, neurološki ispadi, povišena temperatura i oštećenje bubrega. TTP je specifično povezan sa teškim nedostatkom ADAMTS13, specifične proteaze koja cepa von Villebrand faktor. Nedostatak ADAMTS13 se najčešće povezuje sa ADAMTS13 autoantitelima. Terapiju čine izmene plazme, ciklofosfamid, vinkristin ili ciklosporina A; splenektomija ili najnoviji lek kaplacizumab.
Prikaz slučaja: radi se o bolesnici od 49 godina koja je primljena u lošem opštom stanju sa Hgb: 20 g/L, Hct: 0,8 L/L, trombociti: 43 x10^9L, LDH: 2914, AST: 1273 a ALT: 1085, haptoglobin: 0,03 g/L. Bolesnici su primenjene dve jedinice filtrovanih eritrocita, a tokom dana još dve. Urađena je hitna izmena plazme sa volumenom 1,3 uz primenu visokih doza kortikosteroida. Nakon prve izmene plazme došlo je do porasta trombocita na 57x10^9L, uz porast Hgb na 88 g/L, uz pad AST:172 U/L i ALT: 378 U/L. Nakon treće izmene plazme Hgb je bio 112 g/L, Hct: 0,36 L/L, trombociti 108x10^9L, AST:24 U/L i ALT: 97 U/L, a LDH: 532 U/L. Nakon četvrte izmene plazme broj trombocita je bio 164 x10^9L, a LDH: 425 U/L, a nakon pete je broj trombocita bio 264 x10^9L.
Zaključak: brza i pravovremena dijagnostika TTP-a, uz svakodnevne izmene plazme uz kortikosteroide, su doveli do potpunog kliničkog oporavka.

UP 20

RARE BUT URGENT: THROMBOTIC THROMBOCYTOPENIC PURPURA – A CASE REPORT

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Introduction: Thrombotic thrombocytopenic purpura (TTP) is life-threatening thrombotic microangiopathy with hemolytic anemia, severe thrombocytopenia, neurological manifestations, fever, and renal impairment. TTP is associated with a severe deficiency of ADAMTS13. Treatment consists of plasma exchange, cyclophosphamide, vincristine, or cyclosporine A therapy, splenectomy, and the recently introduced agent caplacizumab.
Case Report: A 49-year-old female patient was admitted in poor general condition with hemoglobin (Hb) of 20 g/L, hematocrit (Hct) of 0.08 L/L, platelet count of 43 × 10^9/L, lactate dehydrogenase (LDH) of 2914 U/L, aspartate aminotransferase (AST) of 1273 U/L, alanine aminotransferase (ALT) of 1085 U/L, and haptoglobin of 0.03 g/L. The patient received two units of leukoreduced red blood cells, followed by an additional two units later the same day. Emergency plasma exchange with a plasma volume of 1.3 was performed in combination with high-dose corticosteroid therapy. After the first plasma exchange, the platelet count increased to 57 × 10^9/L, hemoglobin rose to 88 g/L, while AST and ALT decreased to 172 U/L and 378 U/L, respectively. After the third plasma exchange, Hb was 112 g/L, Hct 0.36 L/L, platelet count 108 × 10^9/L, AST 24 U/L, ALT 97 U/L, and LDH 532 U/L. Following the fourth plasma exchange, the platelet count reached 164 × 10^9/L and LDH decreased to 425 U/L, while after the fifth plasma exchange the platelet count increased to 264 × 10^9/L.
Conclusion: Rapid and timely diagnosis of TTP, together with daily plasma exchange and corticosteroid therapy, resulted in complete clinical recovery.
Keywords: apheresis, TTP, plasma exchange.

UP 21

NOVI HLA-C ALEL KOD HEMATOLOŠKOG PACIENTA – PRVI NOVI HLA ALEL IZ SRBIJE

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Odeljenje za tipizacuiju tkiva, Institut za transfuziju krvi Srbije, Beograd Sistem humanih leukocitnih antigena (HLA) predstavlja najpolimorfniji sistem u humanom genomu. Detaljna analiza HLA alela je od ključnog značaja za pronalaženje donora za transplantaciju matičnih ćelija hematopoeze (TMĆH). Cilj ovog rada je da prikaže otkriće prvog novog HLA alela prijavljenog iz Srbije kod hematološko-onkološkog pacijenta koji se pripremao za TMĆH. METODE. Uzorci su dobijeni od muškarca starog 66 godina, bez srodnog donora. Genomska DNK je izolovana iz uzoraka periferne krvi i brisa bukalne sluznice. HLA tipizacija je rađena metodama PCR-SSO (One Lambda) na instrumentu Luminex FLEXMAP 3D, PCR-SSP (CareDx) i sekvenciranjem nove generacije (NGS) pomoću NGSgo-MX11-3 kita na platformi Illumina iSeq100. Aleli su analizirani korišćenjem softvera NGSengine uz reference iz IPD-IMGT/HLA baze podataka v3.55.0. REZULTATI. Rutinskom PCR-SSO tipizacijom nije bilo moguće dobiri rezultat za lokus HLA-C, kao ni metodom PCR-SSP. NGS analiza identifikovala je HLA-C*06:44:01 kao najbliži homologni alel uz sinonimnu nukleotidnu supstituciju u kodonu 47 egzona 2 (CCG→CCC), koja kodira istu aminokiselinu, prolin. Rezultat je potvrđen korišćenjem DNK iz brisa bukalne sluznice. Nova sekvenca je dostavljena u GenBank, a Komitet za nomenklaturu faktora HLA sistema Svetske zdravstvene organizacije dodelio je naziv HLA-C*06:44:02, koji je objavljen u izveštaju IPD-IMGT/HLA baze podataka, verzija 3.58. Nakon završene HLA tipizacije pacijenta, pronađeni su potencijalno odgovarajuće podudarni donori. ZAKLJUČAK. Uvođenje nove tehnike tipizacije HLA omogućilo je otkrivanje prvog novog HLA alela, HLA-C*06:44:02, u Srbiji, kao i uspešan izbor donora za TMĆH.

KLJUČNE REČI: Humani leukocitni antigeni, sekvenciranje sledeće generacije, novi aleli, transplantacija MĆH

UP 21

A NEW HLA-C ALLELE IN A HAEMATOLOGICAL PATIENT – THE FIRST NOVEL HLA ALLELE REPORTED FROM SERBIA

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The system of human leucocyte antigens (HLA) is the most polymorphic human genetic system. Detailed analysis of HLA alleles is essential for searching for donors for haematopoietic stem cell transplantation (HSCT). This study aimed to show the discovery of the first HLA new allele reported from Serbia in a hemato-oncology patient planning for HSCT. METHODS. Samples were obtained from a 66-year-old male patient, without a related donor. Genomic DNA was isolated from peripheral blood and buccal swab samples. HLA typing was performed by PCR-SSO (One Lambda) on the Luminex FLEXMAP 3D instrument, PCR-SSP (CareDx), and next-generation sequencing (NGS) with an NGSgo-MX11-3 kit on the Illumina iSeq100 platform. Allele assignment and phasing were analysed using NGSengine software with references from the IPD-IMGT/HLA Database v3.55.0. RESULTS. On routine PCR-SSO typing, the results of the HLA-C locus were not interpretable. A PCR-SSP did not resolve the typing. NGS analysis identified HLA-C06:44:01 as the closest homologous allele and revealed a synonymous nucleotide substitution in codon 47 of exon 2 (CCG→CCC), encoding the same amino acid, proline. The result was confirmed using DNA from a buccal swab. The novel sequence was submitted to GenBank, and the name HLA-C*06:44:02 has been officially assigned by the WHO Nomenclature Committee for Factors of the HLA System and published on the IPD-IMGT/HLA Database report version 3.58. As the HLA typing of the patient was completed, potentially suitable matched donors were found. CONCLUSION. The introduction of a new technique of HLA typing allowed the detection of the first novel HLA allele, HLA-C*06:44:02, in Serbia, and the successful selection of donors for HSCT.

KEYWORDS Human leucocyte antigen, next-generation sequencing, new allele, haematopoietic stem cell transplantation

UP 22

IMUNOLOŠKA REFRAKTARNOST NA TRANSFUZIJE TROMBOCITA KOD PEDIJATRIJSKE BOLESNICE SA MIJELODISPLASTIČNOM NEOPLAZMOM: ZNAČAJ REGISTRA TIPIZIRANIH DAVALACA AFEREZNIH TROMBOCITA – PRIKAZ SLUČAJA

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Ključne reči: imunološka refraktarnost na transfuzije trombocta, aferezni trombociti, MDS

Mijelodisplastična neoplazma u dečjem uzrastu predstavlja retko hematološko oboljenje u čijoj osnovi je neefektivna hematopoeza praćena citopenijom svih krvnih loza. Ključni deo lečenja predstavlja transfuziološka podrška. Zbrinjavanje trombocitopenije često zahteva višestruke transfuzije trombocita koje mogu dovesti do senzibilizacije te razvoja antitela na humane leukocitne antigene (anti-HLA) i/ili humane trombocitne antigene (anti-HPA) kod bolesnika. Razvija se refraktarnost na transfuzije trombocita posredovana imunološkim mehanizmom sa većim rizikom za hemoragijske komplikacije.
Prikazujemo petnaestogodišnju bolesnicu sa MDS-om i izraženom trombocitopenijom hospitalizovanu radi pripreme za alogenu transplantaciju matičnih ćelija hematopoeze (MĆH) od HLA identičnog srodnog davaoca (sestre). Bolesnica je lečena randomizovanim koncentratima trombocita na koje je razvila refraktarnost. Potvrđeno je prisustvo anti-HLA i anti-HPA antitela Luminex metodom. Dalje transfuziološko lečenje podrazumevalo je primenu tipiziranih koncentrata trombocita. Pretraživanjem postojećeg Registra tipiziranih davalaca afereznih trombocita identifikovano je 10 potencijalnih kompatibilnih davalaca. Uz pisanu saglasnost dodatno su testirana i tipizirana još 43 davaoca, od kojih je 20 (46,5%) bilo kompatibilno sa bolesnicom, primenjena je metoda komplement zavisne citotoksičnosti (CDC). U peritransplantacionom periodu bolesnica je primila 18 transfuzija tipiziranih, filtrovanih afereznih trombocita, krvne grupe 0+(poz) i 0-(neg) bez značajnih komplikacija. Nakon primanja MĆH bolesnica je nastavila da prima tipizirane transfuzije trombocita, poslednju +17-og dana nakon transplantacije. Ovaj prikaz slučaja ističe značaj Registra tipiziranih davalaca afereznih trombocita i naglašava ulogu transfuziologa u lečenju bolesnika sa imunološkom refraktarnošću na transfuzije trombocita u periodu alogene transplantacije MĆH.

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IMMUNE-MEDIATED PLATELET TRANSFUSION REFRACTORINESS IN A PEDIATRIC PATIENT WITH MYELODYSPLASTIC NEOPLASM: THE IMPORTANCE OF A TYPED APHERESIS PLATELET DONOR REGISTRY – CASE REPORT

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Myelodysplastic neoplasm in childhood represents a rare hematological disorder characterized by ineffective hematopoiesis accompanied by cytopenia of all blood cell lineages. A key component of treatment is transfusion support. Management of thrombocytopenia often requires multiple platelet transfusions, which may lead to sensitization and the development of antibodies against human leukocyte antigens (anti-HLA) and/or human platelet antigens (anti-HPA) in patients. This results in transfusion refractoriness mediated by immunological mechanisms, increasing the risk of hemorrhagic complications.
We present a 15-year-old female patient diagnosed with MDS and severe thrombocytopenia, hospitalized for allogeneic hematopoietic stem cell transplantation from a HLA-matched related donor, her sister. The patient had previously been treated with random donor platelet concentrates and subsequently developed platelet transfusion refractoriness. Refractoriness was confirmed by the identification of anti-HLA and anti-HPA antibodies with Luminex test. Further transfusion management included the administration of typed, filtered apheresis platelets. A search of the existing Registry of typed apheresis platelet donors identified 10 potentially compatible donors. In addition, with written informed consent, 43 more donors were tested and typed, 20 (46,5%) were compatible with the patient with Complement-dependent cytotoxicity test (CDC). During the peri-transplant period, the patient received 18 transfusions of typed, apheresis platelets without significant complications. The transplantation procedure was successfully performed, and the last platelet transfusion was administered on day +17 after transplantation. This case report highlights the importance of maintaining a Registry of typed apheresis platelet donors and emphasizes the crucial role of transfusion specialists in the management of patients with immune-mediated platelet transfusion refractoriness during allogeneic hematopoietic stem cell transplantation.
Keywords: immune-mediated platelet refractoriness, apheresis platelets, MDS

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DISTRIBUCIJA HLA-DPB1 T-ĆELIJSKIH EPITOPSKIH GRUPA (TCE) KOD POTENCIJALNIH DAVALACA MATIČNIH ĆELIJA HEMATOPOEZE U SRBIJI: UTICAJ ZA IZBOR PRIHVATLJIVIH DONORA

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Uvod: Kod većine transplantacija hematopoetskih matičnih ćelija prisutna (HSCT) je HLA-DPB1 nepodudarnost između pacijenta i nesrodnog davaoca, koja dugo nije uzimana u obzir pri izboru donora. Radi procene njenog imunološkog značaja razvijen je model T-ćelijskih epitopa (TCE), koji klasifikuje HLA-DPB1 alele u tri funkcionalne grupe. Ovaj model omogućava razlikovanje dozvoljenih i nedozvoljenih nepodudarnosti i danas predstavlja važan alat pri izboru optimalnog nesrodnog davaoca za alogenu HSCT. **Cilj:** Ispitati distribuciju HLA-DPB1 alela i TCE grupa u populaciji potencijalnih davalaca hematopoetskih matičnih ćelija Srbije (RDKS), sa osvrtom na njihov značaj u proceni prihvatljivosti nepodudarnosti i izboru nesrodnih davalaca. **Materijal i metode:** Studija uključuje 1445 davalaca iz Registra davalaca matičnih ćelija hematopoeze Srbije. Uzorci DNK izolovani su automatizovanim metodama Maxwell-16 (Promega, SAD) i SaMag-12 (Sacace, Komo, Italija). HLA tipizacija izvedena je metodama NGS (GenDx, Holandija), dok je sekvenciranje sprovedeno u DKMS Life Science Lab na platformi Illumina NovaSeq 6000. **Rezultati:** DPB1**04:01 (38,89%), DPB1**02:01 (17,54%) i DPB1**04:02 (15,85%) bili su aleli sa najvećom učestalošću u ispitivanoj populaciji. Najučestaliji genotipovi su: HLA-DPB1**02:01, *04:01 (15,08%), HLA-DPB1**04:01, *04:01 (14,25%) i HLA-DPB1**04:01, *04:02 (13,35%). Dominantna TCE grupa bila je grupa 3 sa učestalošću od 84,56%, dok su među TCE genotipovima najčešće kombinacije 3+3 (71,76%) i 2+3 (16,40%). Analiza HLA-DPB1 lokusa pokazala je značajno odstupanje od Hardi-Vajnbergove ravnoteže ($\chi^2 = 4256.22$, $p<0.0001$). **Zaključak:** Rezultati pokazuju dominaciju alela HLA-DPB1*04:01 i genotipova koji ga sadrže među potencijalnim davaocima u Srbiji. Ovakva distribucija predstavlja značajnu osnovu za primenu HLA-DPB1 zasnovanih algoritama u izboru nesrodnih davalaca. Visoka učestalost TCE grupe 3 i genotipa 3+3 može ukazivati na povoljan imunogenetički profil za identifikaciju permisivnih HLA-DPB1 nepodudarnosti.

Ključne reči: HLA-DPB1 tipizacija, TCE (T-ćelijske epitopske grupe), HSCT (transplantacija hematopoetskih matičnih ćelija prisutna), RDKS (Registar davalaca matičnih ćelija hematopoeze Srbije)

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DISTRIBUTION OF HLA-DPB1 T-CELL EPITOPE GROUPS (TCE) AMONG POTENTIAL HEMATOPOIETIC STEM CELL DONORS IN SERBIA: IMPLICATIONS FOR THE SELECTION OF ACCEPTABLE DONORS

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Introduction: In most hematopoietic stem cell transplantations (HSCT), an HLA-DPB1 mismatch between the patient and the unrelated donor is present and was long not considered during donor selection. To assess its immunological significance, the T-cell epitope (TCE) model was developed, classifying HLA-DPB1 alleles into three functional groups. This model enables differentiation between permissive and non-permissive mismatches and is now considered an important tool in selecting the optimal unrelated donor for allogeneic HSCT. **Aim:** To investigate the distribution of HLA-DPB1 alleles and TCE groups in the population of potential hematopoietic stem cell donors in Serbia (RDKS), with particular emphasis on their significance in assessing mismatch permissiveness and selecting unrelated donors. **Materials and Methods:** The study included 1,445 donors from the Serbian Hematopoietic Stem Cell Donor Registry. DNA samples were isolated using automated methods Maxwell-16 (Promega, USA) and SaMag-12 (Sacace, Como, Italy). HLA typing was performed using NGS methods (GenDx, Netherlands), while sequencing was conducted at the DKMS Life Science Lab using the Illumina NovaSeq 6000 platform. **Results:** DPB1**04:01 (38.89%), DPB1**02:01 (17.54%), and DPB1**04:02 (15.85%) were the most frequent alleles in the studied population. The most common genotypes were HLA-DPB1**02:01*, *04:01 (15.08%), HLA-DPB1**04:01, *04:01 (14.25%), and HLA-DPB1**04:01, *04:02 (13.35%). The dominant TCE group was group 3, with a frequency of 84.56%, while among TCE genotypes, the most frequent combinations were 3+3 (71.76%) and 2+3 (16.40%). Analysis of the HLA-DPB1 locus showed a significant deviation from Hardy–Weinberg equilibrium ($\chi^2 = 4256.22$, $p < 0.0001$). **Conclusion:** The results demonstrate the predominance of the HLA-DPB1*04:01 allele and genotypes containing it among potential donors in Serbia. This distribution provides an important basis for the implementation of HLA-DPB1-based algorithms in unrelated donor selection. The high frequency of TCE group 3 and the 3+3 genotype may indicate a favorable immunogenetic profile for identifying permissive HLA-DPB1 mismatches.

Keywords: HLA-DPB1 typing, TCE (T-cell epitope groups), HSCT (hematopoietic stem cell transplantation), RDKS (Registry of hematopoietic stem cell donors of Serbia)

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RHD ALELI IDENTIFIKOVANI U TROGODIŠNJEM PERIODU U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE

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Uvod: Prema aktuelnoj ISBT bazi podataka pored referentnog alela na RDH lokusu su opisana i 172 slaba D, 136 parcijalna D, 45 Del i 92 tiha alela.

Cilj: Prikazati učestaosti RHD alela u odnosu na serološki Rh fenotip.
Metod: Izvršena je retrospektivna analiza podataka iz protokola u periodu 2023.-2025. Izolacija DNK rađena je manuelno iz periferne krvi uzete u epruvete na EDTA pomoću QIAamp DNA Blood Mini Kit (QIAGEN, Nemačka). Genotipizacija je rađena RealTime-PCR metodom na aparatu FluoQube, korišćenjem testova RBC-FluoGene D® weak/variant, RBC-FluoGene® CDE i RBC-FluoGene® CDE eXtend (Inno-train Diagnostik GmbH, Nemačka).
Rezultati: Analizirano je 110 uzoraka koji su označeni kao „serološki slabo D“ i 33 uzorka kod kojih serološkim metodama nije bilo moguće dokazati prisustvo RhD antigena, ali su u Rh fenotipu osobe bile C-pozitivne i/ili E-pozitivne. Kod jedne osobe serološki označene kao RhD-negativne dokazan je alel RHD*11. Jedna osoba je imala alel RHD*01N.04 sa fenotipom CCddee.
Kod ispitanika fenotipa CcD^{w}ee (79) najčešće dokazani aleli bili su: RHD*01W.01 u 42, RHD*11 u 13, RHD*01W.03 u 11 i referentni alel u 5 slučajeva. Kod ispitanika fenotipa CCD^{w}ee (15) pronađeni su aleli RHD*01W.01 u 7, RHD*01W.03 u 3 i referentni alel u 4 slučaja. Kod 50% ispitanika fenotipa ccD^{w}Ee (6) bio je prisutan RHD*01W.02 alel. Bilo je po 5 ispitanika fenotipova ccD^{w}ee i CcD^{w}Ee, u obe grupe referentni alel identifikovan je u po 3 slučaja.
Zaključak: Sistematski primena genotipizacije RHD gena olakšava transfuziološko zbrinjavanje pacijenata sa „serološki slabim D“ i povećati sigurnost transfuzije eritrocita identifikacijom davalaca Del fenotipa.
Ključne reči: Rh sistem, RHD aleli, RH genotipizacija, transfuzijska medicina

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RHD ALLELES IDENTIFIED IN A THREE-YEAR PERIOD AT THE BLOOD TRANSFUSION INSTITUTE OF SERBIA

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Background: The ISBT Blood Group Database documents 172 weak D, 136 partial D, 45 Del, and 92 null RHD alleles alongside the reference allele.
Aim: This study correlates RHD allele frequencies with serological Rh phenotypes.
Methods: A retrospective analysis (2023–2025) was performed. DNA was manually extracted from peripheral blood using the QIAamp DNA Blood Mini Kit (QIAGEN, Germany). Genotyping utilized RealTime-PCR on the FluoQube apparatus with RBC-FluoGene D weak/variant, CDE, and CDE eXtend tests (Inno-train Diagnostik GmbH, Germany).
Results: The study analyzed 110 “serologically weak D” samples and 33 serologically RhD-negative samples that were C-positive and/or E-positive. One serologically RhD-negative individual carried the RHD*11 allele, and another carried the RHD*01N.04 allele (CCddee phenotype). Among 79 CcDwee individuals, the most frequent alleles were RHD*01W.01 (42), RHD*11 (13), RHD*01W.03 (11), and the reference allele (5). In 15 CCDwee individuals, RHD*01W.01 (7), RHD*01W.03 (3), and the reference allele (4) predominated. Half of the ccDwEe (6) subjects possessed the RHD*01W.02 allele. Five individuals each had ccDwee and CcDwEe phenotypes, with the reference allele found in three cases per group.
Conclusion: Systematic RHD genotyping optimizes transfusion care for “serologically weak D” patients and enhances erythrocyte transfusion safety by identifying Del phenotype donors.
Keywords: Rh system, RHD alleles, RH genotyping, transfusion medicine

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„SAVREMENI MONITORING TRUDNOĆE IZAZVANE RHD-ALOIMUNIZACIJOM PRIMENOM RHD GENOTIPIZACIJE FETUSA – PRIKAZ SLUČAJA”

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Uvod: Hemolizna bolest fetusa i novorođenčeta (HBFN) i dalje predstavlja značajan problem u perinatalnoj zdravstvenoj zaštiti. Uzrokovana je najčešće anti-D aloantitelima majke protiv RhD antigena fetusa. Neinvazivna RHD genotipizacija fetusa u trudnoćama svih RhD-negativnih žena koje imaju RhD-pozitivne partnere, određivanje zigotnosti RHD gena oca, serološka imunohematološka testiranja majke u trudnoći, ultrazvučna dijagnostika brzine protoka krvi kroz arteriju cerebri media-u fetusa i intrauterine transfuzije, sastavni su deo savremenog monitoringa rizičnih trudnoća sa aloimunizacijama.
Prikaz slučaja: Trudnica, u dobi od 31 godine, u 4. nedelji četvrte trudnoće javila se Odeljenju za imunohematološka ispitivanja ITKS. Skrining i identifikacija pokazali su prisustvo anti-D antitela enzimskom tehnikom i u IAT, metodom u gelu. Titar anti-D antitela na prvoj kontroli je 128 u IAT automatizovanom metodom u gelu, a 64 metodom u epruveti, što se ne smatra signifikantnom razlikom. Anamnestički, prva trudnoća završena rođenjem živorođenog deteta, sa znacima žutice, bez primene transfuzija eritrocita, druga trudnoća namerno prekinuta, treća trudnoća sa znacima anemije i žutice, dete dobilo dve transfuzije eritrocita. Rh zaštita primenjena posle prekida druge trudnoće. U aktuelnoj trudnoći titar anti-D antitela u kasnijim kontrolama se kretao se od 128 do 1024 u IAT, podjednako u obe metode. Genotipizacijom je utvrđena homozigotnost oca za RHD gen, a za fetus da je RHD-pozitivan. U Centru za rizične trudnoće se vrši kontinuirani stručni monitoring trudnoće trenutno u 24. nedelji gestacije, a intrauterine trasfuzije još nisu primenjivane.
Zaključak: Integrisano serološko, molekularno i ultrazvučno praćenje trudnice i ploda su neophodni činioci u proceni rizika i pravovremenom vođenju RhD-aloimunizovane trudnoće.
Ključne reči: hemolizna bolest fetusa i novorođenčeta, neinvazivna prenatalna dijagnostika, aloimunizacija

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CURRENT MONITORING OF HEMOLYTIC DISEASE OF THE FETUS AND NEWBORN IN THE LIGHT OF RHD GENOTYPING AND TARGETED IMMUNOPROPHYLAXIS – CASE REPORT

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Introduction: Hemolytic disease of the fetus and newborn (HDFN) continues to represent a significant issue in the perinatal health protection. It is most commonly caused by anti-D antibodies of the mother against RhD antigens of the fetus. Non-invasive RHD genotyping of the fetus in pregnancies of all RhD-negative women with PhD-positive partners, determination of the zygosity of RHD gene of the father, serological immunohematology testing of the mother during pregnancy, ultrasound diagnostics of the blood flow speed through the artery of cerebri media of the fetus and intrauterine transfusion, represent an integral part of the modern monitoring of risky pregnancies with alloimmunizations.
Case report: Pregnant woman, 31 years of age, in the 4th week of gestation was admitted to the immunohematology testing department of the BTIS. Screening and identification showed presence of anti-D antibodies by way of enzyme method and in IAT, using gel method. Titer of anti-D antibodies was 128 in IAT automated method in gel, with 64 method in test tube, which is not considered significant difference. Regarding medical history, the first pregnancy ended with a live-born infant, with signs of jaundice, without the application erythrocyte transfusion, the second pregnancy was terminated deliberately, the third one was with signs of anemia and jaundice, the child received two erythrocyte transfusions. Rh protection applied after the termination of the second pregnancy. In the current pregnancy titer of anti-D antibodies during later controls moved from 128 to 1024 in IAT, equally in both methods. Genotyping determined homozygosity of the father for RHD gene, and the fetus was RHD positive. Continuous professional monitoring is performed in the center for risky pregnancies. Currently she is in the 24th week of gestation, intrauterine pregnancies are not yet applied.
Conclusion: Integrated serological, molecular and ultrasound monitoring of the pregnant woman and fetus are mandatory factors in the risk assessment and timely management of RhD- alloimmunized pregnancy.
Key words: hemolytic disease of the fetus and newborn, non-invasive prenatal diagnostics, alloimmunization

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ANTI-G ANTITELO U TRUDNOĆI: KAD POSUMNJATI? ŠTA SMO NAUČILI?

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UVOD: Antigen G je prisutan kod gotovo svih osoba sa D i/ili C antigenom. RhD-negativne osobe mogu da stvore anti-G antitelo koje serološki često daje sliku anti-D+ anti-C antitela.
CILJ: Prikaz trudnoće u kojoj smo dokazali anti-G antitelo i rođenja deteta sa jako pozitivnim DAT-om i blagom HBFN.
PRIKAZ SLUČAJA: Trudnicu M.T. (37 godina) smo redovno kontrolisali od 16. ng. treće trudnoće. Nakon prethodne primila je RhD imunoprofilaksu. KG: AB RhD-negativan, ccddee. IAT: anti-D+C antitela. KG supruga: O RhD-pozitivan, CCDee. Do porođaja titar prividnog anti-D antitela kretao se od 1 do 4, titar prividnog anti-C antitela od 8 do 16. Ultrazvučne kontrole biofizičkog profila fetusa i brzine protoka krvi kroz A.C.M. rađene su najmanje dva puta nedeljno i uvek su bile uredne. U 26. ng je tehnikom dvostruke adsorpcije i elucije dokazano postojanje jedino anti-G antitela. U 28. ng je primila RhD imunoprofilaksu. Porođaj je sproveden carskim rezom u 38. ng, rođeno je zdravo žensko novorođenče, KG: B RhD-pozitivan, CcDee, DAT 3+, Apgar 9/10. Nultog dana ukupni bilirubin: 84,6 μmol/L (referentno < 103,0), direktni 4,7 μmol/L (< 3,4), Hb 172 g/L. Sprovedena je fototerapija; prvog dana: ukupni bilirubin 122,3, direktni 6,8; drugog dana ukupni bilirubin 116,9, direktni 5,4. Porodilja je dobila RhD imunoglobulin nakon porođaja.
ZAKLJUČAK: Na anti-G antitelo treba posumnjati ako su RhD-negativne trudnice razvile anti-D antitelo iako su primile RhD imunoglobulin nakon prethodnog porođaja; kada imaju anti-C+D antitela a titar anti-C je veći od anti-D, kada titrovi ne rastu značajno.
KLJUČNE REČI: anti-G antitelo, DAT.

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ANTI-G ANTIBODY IN PREGNANCY: WHEN SHOULD IT BE SUSPECTED? WHAT HAVE WE LEARNED?

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INTRODUCTION: The G antigen is present in almost all persons who express the D and/or C antigen. RhD-negative individuals may develop anti-G antibodies, which serologically often mimic the presence of both anti-D and anti-C antibodies.
OBJECTIVE: To present a pregnancy in which anti-G antibody was confirmed and the birth of a newborn with a strongly positive DAT and mild HDFN.
CASE REPORT: A 37-year-old pregnant woman M.T. was regularly monitored at our Clinic from the 16th wg in her third pregnancy. After a previous pregnancy, she had received RhD immunoprophylaxis. Blood group: AB RhD-negative, ccddee. IAT: anti-D and anti-C antibodies. Husband’s blood group: O RhD-positive, CCDee. Until delivery, the „like anti-D antibody” titer ranged from 1 to 4, while the „like anti-C antibody” titer ranged from 8 to 16. Ultrasound monitoring of the fetal biophysical profile and M. C. A. peak systolic velocity was performed at least twice weekly and remained within normal limits throughout the pregnancy. At 26 wg, only anti-G antibody was demonstrated using the double adsorption and elution technique. RhD immunoprophylaxis was administered at 28 wg. Delivery was performed by cesarean section at 38 wg. A healthy female newborn was delivered with blood group B RhD-positive, CcDee, DAT 3+. Apgar score was 9/10. On day 0, total bilirubin was 84.6 μmol/L (reference <103.0), direct bilirubin 4.7 μmol/L (reference <3.4), Hb 172 g/L. Phototherapy was initiated. On day 1, total bilirubin was 122.3 μmol/L and direct bilirubin 6.8 μmol/L; on day 2, total bilirubin was 116.9 μmol/L and direct bilirubin 5.4 μmol/L. The mother received RhD immunoglobulin postpartum.
CONCLUSION Anti-G antibody should be suspected if RhD-negative pregnant women develop anti-D antibody despite receiving RhD immunoglobulin after a previous delivery; when they have anti-C+D antibodies and the titer of anti-C is higher than anti-D, when the titers do not increase significantly.
KEYWORDS: anti-G antibody, DAT.

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KOMBINOVANA ANTI-D I ANTI-S ALOIMUNIZACIJA U TRUDNOĆI – PRIKAZ SLUČAJA

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Uvod Aloimunizacija eritrocitnim antigenima u trudnoći predstavlja značajan uzrok hemolitičke bolesti fetusa i novorođenčeta (HDFN). Uvođenje RhD imunoprofilakse drastično je smanjilo učestalost anti-D senzibilizacije, ali ne pruža zaštitu od senzibilizacije na ne-D antigene, poput anti-S antitela iz MNS sistema, koje se sreće kod svega oko 2% trudnica sa pozitivnim skriningom. Kombinovana anti-D i anti-S aloimunizacija izuzetno je retka i opisana samo u pojedinačnim slučajevima u svetskoj literaturi.
Prikaz slučaja Prikazujemo slučaj 31-godišnje RhD-negativne trudnice, u drugoj trudnoći, komplikovanoj kombinovanom anti-D i anti-S senzibilizacijom, kod koje antenatalna RhD profilaksa u prethodnoj trudnoći nije primenjena. Antitela su otkrivena u 22. nedelji gestacije (anti-D 1:16, anti-S u niskom titru), uz porast anti-D titra do maksimalnih 1:256, dok je titar anti-S antitela ostao stabilan. Porođaj je završen elektivnim carskim rezom; novorođenče (fenotip CcDee, Ss) imalo je pozitivan direktni antiglobulinski test (4+), hiperbilirubinemiju i progresivan pad hemoglobina, usled čega su primenjeni fototerapija, intravenski imunoglobulin i transfuzija fenotipski usklađene, S-negativne eritrocitne mase. Kontrola u trećem mesecu života pokazala je potpuno uredan nalaz.
Zaključak Kombinovana anti-D i anti-S aloimunizacija predstavlja redak, ali klinički značajan izazov, pri čemu anti-S antitelo nosi rizik od kasne neonatalne anemije i ograničene pouzdanosti ultrazvučnog (MCA Doppler) monitoringa. Dosledna primena antenatalne RhD profilakse, sistematski skrining na iregularna antieritrocitna antitela i pravovremena, fenotipski usklađena transfuziološka podrška ključni su za bezbedan ishod ovakvih trudnoća.
Ključne reči: aloimunizacija, anti-D, anti-S, HDFN, RhD profilaksa, MNS sistem, DAT, transfuzija.

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COMBINED ANTI-D AND ANTI-S ALLOIMMUNIZATION IN PREGNANCY – A CASE REPORT

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Introduction Red blood cell alloimmunization in pregnancy is an important cause of hemolytic disease of the fetus and newborn (HDFN). The introduction of RhD immunoprophylaxis has dramatically reduced the incidence of anti-D sensitization, but it offers no protection against sensitization to non-D antigens, such as anti-S antibodies of the MNS blood group system, found in only about 2% of pregnant women with a positive antibody screen. Combined anti-D and anti-S alloimmunization is exceptionally rare and has been described only in isolated case reports in the world literature.
Case report We present the case of a 31-year-old RhD-negative woman in her second pregnancy, complicated by combined anti-D and anti-S sensitization, in whom antenatal RhD prophylaxis had not been administered during the previous pregnancy. Antibodies were detected at 22 weeks of gestation (anti-D titer 1:16, anti-S at a low titer); the anti-D titer subsequently rose to a maximum of 1:256, while the anti-S antibody titer remained stable. Delivery was completed by elective cesarean section; the newborn (phenotype CcDee, Ss) had a positive direct antiglobulin test (4+), hyperbilirubinemia, and a progressive decline in hemoglobin, requiring phototherapy, intravenous immunoglobulin, and transfusion of phenotype-matched, S-negative red blood cells. Follow-up at three months of age showed a completely normal finding.
Conclusion Combined anti-D and anti-S alloimmunization is a rare but clinically significant challenge, with anti-S antibodies carrying a risk of late neonatal anemia and limited reliability of ultrasound (MCA Doppler) monitoring. Consistent implementation of antenatal RhD prophylaxis, systematic screening for irregular red-cell antibodies, and timely, phenotype-matched transfusion support are essential for a safe outcome in such pregnancies.
Keywords: alloimmunization, anti-D, anti-S, HDFN, RhD prophylaxis, MNS system, DAT, transfusion.

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KLINIČKI TOK HEMOLIZNE BOLESTI FETUSA I NOVOROĐENČETA UZROKOVANE VIŠESTRUKIM ANTITELIMA

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Uvod: Hemolizna bolest fetusa i novorođenčeta (HBFN) najčešće je posledica ABO i Rh inkompatibilije, Prisustvo višestrukih antieritrocitnih antitela je retko, ali predstavlja dijagnostički i terapijski izazov zbog različitog kliničkog toka bolesti.
Cilj: Prikazati klinički tok i imunohematološke karakteristike HBFN uzrokovane višestrukim antitelima, kroz seriju tri slučaja.
Materijal i metode: Analizirana su tri slučaja HBFN izazvana kombinacijom Rh i non-Rh antieritrocitnih antitela, dijagnostikovana u Institutu za transfuziju krvi Srbije. Analizirani su klinički tok, imunohematološki nalazi i terapijski pristup.
Rezultati: Kod zdrave prvorotke u 26. nedelji, zbog zastoja u rastu ploda, postavljena je sumnja na HBFN. Identifikovana su anti-Jka, anti-s i suspektno anti-Kel antitelo u niskom titru. Dete je rođeno u 32.gestacijskoj nedelji sa znacima teške hemolize. Primenjene su višestruke transfuzije, uz produženu hospitalizaciju i nepovoljnu dugoročnu prognozu. U drugom slučaju tokom trudnoće identifikovana su anti-Cw i anti-E antitela u titrovima 2 i 4. Novorođenče rođeno u 31. gestacijskoj nedelji imalo je blagu HBFN, lečeno fototerapijom i transfuzijom eritrocita tokom prvog meseca života. U trećem slučaju zbog izostanka prenatalnog skrininga, dijagnoza je postavljena tek nakon rođenja. Tokom rutinskog pregleda u prvom mesecu života utvrđeni su anemija i ikterus uz visoku koncentraciju bilirubina. Imunohematološkim ispitivanjem uz primenu dodatnih metoda, adsorpcijom i elucijom identifikovana su anti-c, anti-E i topla autoantitela.
Zaključak: Klinički tok HBFN uzrokovane višestrukim antitelima može značajno varirati-od blagih do teških oblika. Težina bolesti ne zavisi isključivo od broja prisutnih antitela, već od njihove specifičnosti i međusobne kombinacije. Detaljna imunohematološka obrada ključna je za procenu rizika i dijagnozu.
Ključne reči: hemolizna bolest fetusa i novorođenčeta (HBFN), aloimunizacija, višestruka antieritrocitna antitela.

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CLINICAL COURSE OF HEMOLYTIC DISEASE OF FETUS AND NEWBORN CAUSED BY MULTIPLE ANTIBODIES

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Introduction: Hemolytic disease of the fetus and newborn (HDFN) is most commonly caused by ABO and Rh incompatibility. The presence of multiple red blood cell antibodies is rare, but represents a diagnostic and therapeutic challenge due to the variable clinical course of the disease.
Objective: To present the clinical course and immunohematological characteristics of HDFN caused by multiple antibodies throught a series of three cases.
Materials and Methods: Three cases of HDFN caused by a combination of Rh and non-Rh antibodies diagnosed at the Blood Transfusion Institute of Serbia were retrospectively analyzed. Clinical course, immunohematological findings and therapy were evaluated.
Results: In the first case, HDFN was suspected in healthy primigravida at 26 weeks of gestation due to fetal growth restriction. Anti-Jka, anti-s and suspected anti-Kel were identified at low titers. The infant was born in 32 week of gestation with signs of severe hemolysis. Multiple red blood cell transfusions were required, followed by prolonged hospitalization and unfavorable long-term outcomes. In the second case, anti-Cw and anti-E antibodies with titers 2 and 4 respectively were detected during pregnancy. The newborn delivered at 31 weeks of gestation had mild HDFN and was treated with phototherapy and transfusions, during the first month of life. In the third case, due to the absence of prenatal antibody screening, the diagnosis was established after birth. During a routine examination in the first month of life, anemia and jaundice associated with elevated bilirubin level were detected. Extended immunohematological investigation, including adsorption and elution techniques, identified anti-c, anti-E and warm autoantibodies.
Conclusion: The clinical course of HDFN caused by multiple antibodies may vary ranging from mild to severe disease. Disease severity depends not only on numbers of antibodies present but also on their specificity and interactions. Comprehensive immunological investigation is essential for accurate diagnosis and treatment.
Key words: Hemolytic disease of the fetus and newborn (HDFN), alloimmunisation, multiple red blood cell antibodies

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KOMPARATIVNA ANALIZA ODREĐIVANJA TITRA ANTIERITROCITNIH ANTITELA KOD TRUDNICA

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Uvod: Praćenje titra antieritrocitnih antitela značajno je za uvođenje monitoringa u aloimunizovanim rizičnim trudnoćama. U rutinskom radu zlatni standard je manuelna metoda titracije u epruveti, dok se sve češće koriste automatizovane metode u gelu.**Cilj:** Prikazati komparativnu analizu rezultata titracije antieritrocitnih antitela u uzorcima seruma aloimunizovanih trudnica, dobijenih metodom u epruveti i automatizovanom metodom u gelu.
Materijal i metode: U retrospektivnu studiju uključene su 54 aloimunizovane trudnice sa klinički značajnim antitelima na Odeljenju za imunohematološka ispitivanja ITKS. Titar antitela određivan je manuelnom metodom u epruveti i automatizovanom mikrometodom u gelu. Statistička analiza sprovedena je u programu IBM SPSS Statistics primenom Spearmanove korelacije, Bland–Altman analize i Wilcoxonovog testa, dok je povezanost titra sa kliničkim ishodima procenjivana neparametrijskim testovima i logističkom regresijom.**Rezultati:** Analizirani su rezultati ispitivanja titra 172 uzorka praćenih trudnica. Najčešće detektovano antitelo bilo je anti-D (oko 60% merenja), dok su anti-C i anti-c činili približno 30%uzorka. Dominiraju vrednosti od 32–64, dok se titrovi ≥256 javljaju ređe. Nije utvrđena statistički značajna razlika u vrednostima titra između metoda (p = 0,567), pri čemu su se razlike u najvećem broju slučajeva kretale za najviše jedno do dva dvostruka razblaženja titra, što se ne smatra signifikantnim. Utvrđena je jaka pozitivna korelacija između metoda (Spearman ρ=0,970;p<0,001). Bland-Altman analiza pokazala je srednju razliku od 0,03±0,78 log2 jedinica, bez sistemske pristrasnosti. **Zaključak:** Automatizovana metoda u gelu pokazala je visoku saglasnost sa manuelnom metodom u epruveti uz veću analitičku osetljivost, bolju mogućnost standardizacije i sigurniji način očitavanja rezultata aglutinacije. Za pouzdanu interpretaciju dinamike titra preporučuje se korišćenje obe metode do sticanja većeg iskustva u praksi.
Ključne reči: aloimunizacija u trudnoći, antieritrocitna antitela, titar antitela, metoda u gelu, automatizovana metoda

UP 29

COMPARATIVE ANALYSIS OF RED CELL ANTIBODY TITER DETERMINATION IN PREGNANT WOMEN

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Introduction: Monitoring antierythrocyte antibodies titer is important for the introducing monitoring in alloimumunized high-risk pregnancies. In routine work, the gold standard is the manuel method of titration in a test tube, while automated methods in gel are increasingly used.
Objective: To present a comparative analysis of the results of titration of antierythrocyte antibodies in serum semples of alloimunize pregnant woman, obtained by the test tube method and the automated gel method.
Materials and methods: A retrospective study included 54 alloimunized pregnant woman with clinically significant antibodies at the Department of Immunohematology Testing of ITKS. The antibody titer was determined by a manual method in a test tube and an automated micromethod in a gel. Statistic analysis was performed using the IBM SPSS Statistics program using Spearman correlation, Bland-Altman analysis and Wilcoxon test, while the associatin of titers with clinical outcomes was assessed by non-parametric tests and logistic regression. Results: Results from 172 samples of monitoring pregnancies were analyzed. The most frequently detected antibody was anti-D (about 60% of measurements), while anti-C and anti-c accounted for approximately 30% of the sample. Values of 32-64 dominate, while titers ≥256 occur less often. There was no statistically significant difference in titer values between the methods (p= 0.567), where the differences in most cases ranged from one to two double dilutions of the titer, which is not considered significant. A strong positive correlation has been established between the methods (Spearman ρ=0,970;p<0,001).The Bland-Altman analysis showed a mean difference of 0,03±0,78 log2 units, without systematic bias Conclusion: The automated method in the gel showed a high agreement with the manual method in the test tube with greater analytical sensitivity, better possibility of standardization and safer way of reading the agglutination results. For a reliable interpretation of titer dynamics, it is recommended to use both methods until gaining more experience in practice.
Key words: alloimunization in pregnancy, antierytrocyte antibodies, antibody titer, gel method, automated method

UP 30

DOES POSITIVE DAT ALWAYS SUGGEST CLINICALLY SIGNIFICANT RISK (CASE REPORTS)

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Introduction: A positive direct antiglobulin test (DAT) result confirms that red blood cells are coated with antibodies and/or complement. However, it raises practical questions about the hemolytic potential of the antibodies and the severity of hemolysis concerning the IgG subclasses. According to literature, HDFN cases with IgG1 and IgG3 have more severity compared to IgG2 and IgG4.
Aim: The aim of this study was to investigate the impact of anti-D IgG subclasses to the intensity of hemolysis in cases with HDFN, autoimmune hemolytic anemia (AIHA) and in healthy blood donors.
Material and methods: Pregnant women, second pregnancy with RhD prophylaxes in first pregnancy after huge bleeding during delivery. Immunohematology testing in the beginning of second pregnancy showed sensibilization with anti-D antibody in titer 1:512, raising during pregnancy to 1:4098. All obstetrical checking ups were without fetal anemia. The Newborn was with mild anemia, solved only with Phototherapy in 34 g.w. Second case of pregnant women with anti-D antibodies was with titer of 1:2048 and delivered healthy baby in 35 g.w. Third case was a boy, 8 years old, who was hospitalized with long lasting anemia and severe hemolysis in spite immunosuppressive therapy. DAT (IgG+C3d) was 4+ positive. Three healthy regular blood donors with positive DAT were also included in the study.
In all DAT positive cases we analyzed the IgG subclasses with monoclonal anti-IgG1 and anti-IgG3 in titer 1:1 and 1:100 using BioRad ID-Card with two dilutions of both anti-IgG1 and IgG3, used to differentiate between low and high risk for hemolysis.
Results. In the first case of pregnant women the analyses for the IgG subclasses showed the presence of IgG1 and IgG3 in dilutions 1:1 and 1:100 while in the second case only IgG1 (1:100) was confirmed. In the third, AIHA, case subclasses IgG1 and IgG3 in 1:100 dilution was found.
Blood donor subclasses test results confirmed the presence of IgG1 (1:1 dilution) in one donor, while in the other two donors the presence of subclasses IgG1 and IgG3 was not confirmed.
Conclusion: According to literature, cases with IgG1 and IgG3 have more severity compared to IgG2 and IgG4. Although the presence of IgG1 and IgG3 in mothers, there was no clinically significant hemolysis in the newborns. In the case of AIHA the high-dilution presence of IgG1 and 3 subclasses corresponded to the severity of the hemolysis observed. More investigations and more laboratory testing are needed for better understanding of the complex nature of red blood cell antibodies and the biologic mechanisms involved in immune hemolysis.
Keywords: DAT, risk, hemolysis, IgG1, IgG3

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PREVENTIVNO PROŠIRENO ERITROCITNO FENOTIPIZIRANJE/GENOTIPIZIRANJE KOD HEMATONKOLOŠKIH BOLESNIKA-LUKSUZ ILI POTREBA?

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Uvod: Aloimunizacija predstavlja značajnu komplikaciju kod višestruko transfundiranih bolesnika oboljelih od hematonkoloških oboljenja. Standardna transfuzijska obrada u našoj ustanovi, do ovog trenutka, ne uključuje rutinsko određivanje proširenog antigenskog profila. Aloimunizacija je najčešći razlog za prolongiranje transfuzije usljed otežanog pronalaženja kompatibilne krvi. Mnogi transfuzijski centri rade početno prošireno testiranje prije prve transfuzije i izdavanje Rh (C,c,E,e) i Kell kompatibilnih eritrocita kod bolesnika za koje se očekuje veliki broj transfuzija, iako ne postoje univerzalne preporuke za prošireno eritrocitno tipiziranje.
Cilj: Analizirati dostupne dokaze o ulozi proširenog fenotipiziranja/genotipiziranja i profilaktičkog antigen matchinga u prevenciji aloimunizacije kod hematonkoloških bolesnika, uz prikaz aloimunozacija u šestomjesečnom periodu na Odsjeku za transfuzijsku medicinu prema dg i frekvenci antitijela.
Metode: Pregled relevantne stručne i naučne literature dostupne putem interneta i podaci iz transfuzijskog IS Renovatio Odsjeka za transfuzijsku medicinu.
Rezultati: Pregled dostupne literature pokazuje da rutinsko prošireno antigeno tipiziranje nije indicirano kod svih hematološko-onkoloških pacijenata. Uz oboljenja gdje je prošireno tipiziranje neophodno, preporučuje se kod pacijenata sa aloantitijelima ili kod kojih se očekuje dugotrajna transfuzijska terapija.Za prvih pet i pol mjeseci 2026. godine, od 60 aloimunizovanih pacijenta na našem Odsjeku, 10 pacijenata (16,7%) su hematonkološki pacijenti. Najčešće identifikovana antijela su iz Rh Sistema (5), anti-M (2), anti-K (1) i antitijela neutvrđene specifičnosti (2).
Zaključak: Odluka o provođenju proširenog eritrocitnog antigenog tipiziranja kod hematološko-onkoloških pacijenata treba biti individualizirana i zasnovana na očekivanoj transfuzijskoj izloženosti, prethodnoj aloimunizaciji i procijenjenom riziku od razvoja novih aloantitijela. Potrebno je napraviti stručne preporuke / nacionalne smjernice u cilju zaštite pacijenata i pravovremenog obezbjeđivanju krvi kao lijeka.

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PREVENTIVE EXTENDED ERYTHROCYTE PHENOTYPING/GENOTYPING IN HEMATOONCOLOGICAL PATIENTS - LUXURY OR NECESSITY?

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Introduction: Alloimmunization is a significant complication in multiple transfused patients with hematooncological diseases. Standard transfusion workup in our institution, to date, does not include routine determination of the extended antigen profile. Alloimmunization is the most common reason for prolonging transfusion due to difficulty finding compatible blood. Many transfusion centers perform initial extended testing before the first transfusion and issue Rh (C,c,E,e) and Kell compatible erythrocytes in patients for whom a large number of transfusions are expected, although there are no universal recommendations for extended erythrocyte typing.
Objective: To analyze the available evidence on the role of extended phenotyping/genotyping and prophylactic antigen matching in the prevention of alloimmunization in hematooncology patients, with a presentation of alloimmunizations in a six-month period at the Department of Transfusion Medicine according to dg and antibody frequency.
Methods: Review of relevant professional and scientific literature available via the Internet and data from the transfusion IS Renovatio of the Department of Transfusion Medicine.
Results: A review of the available literature shows that routine extended antigen typing is not indicated in all hematological-oncological patients. In diseases where extended typing is necessary, it is recommended in patients with alloantibodies or in whom long-term transfusion therapy is expected.
For the first five and a half months of 2026, out of 60 alloimmunized patients at our Department, 10 patients (16.7%) were hematooncology patients. The most commonly identified antibodies are from the Rh System (5), anti-M (2), anti-K (1) and antibodies of undetermined specificity (2).
Conclusion: The decision to perform extended erythrocyte antigen typing in hematological-oncological patients should be individualized and based on the expected transfusion exposure, previous alloimmunization and the estimated risk of developing new alloantibodies. Expert recommendations / national guidelines should be made in order to protect patients and ensure timely provision of blood as a medicine.

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SAVREMENI PRISTUPI U PREVAZILAŽENJU INTERFERENCIJE ANTI-CD38 TERAPIJE U PRETRANSFUZIJSKOM TESTIRANJU: SCD38 ILI DTT ?

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Uvod: Anti-CD38 monoklonska antitela, kao što je lek daratumumab, koriste se u lečenju multiplog mijeloma. Vezivanjem za antigen CD38 na površini eritrocita, izazivaju panreaktivnost u indirektnom antiglobulinskom testu. Takva interferencija otežava skrining, identifikaciju eritrocitnih aloantitela i izvođenje unakrsnog testa. Upotreba reagensa ditiotreitola (DTT) predstavlja standardnu metodu za uklanjanje ove interferencije. Za razliku od DTT reagensa, primena reagensa sCD38 ne dovodi do oštećenja eritrocitnih antigena, čime se omogućava očuvanje njihove serološke reaktivnosti.
Cilj: Prikazati značaj i efikasnost sCD38 reagensa u neutralizaciji interferencije anti-CD38 terapije i uporediti njegove karakteristike sa DTT reagensom u pretransfuzijskom testiranju.
Materijal i metodi: Analizirani su uzorci seruma 11 pacijenata sa multiplim mijelomom, lečenih daratumumabom. Neutralizacija interferencije sprovedena je upotrebom sCD38 reagensa prema uputstvu proizvođača (Grifols, Španija), nakon čega su izvršeni skrining, identifikacija antitela i testovi kompatibilnosti primenom standardnih imunohematoloških metoda. Dobijeni rezultati su upoređeni sa rezultatima dobijenim upotrebom DTT reagensa (BioRad, Francuska).
Rezultati: sCD38 je uspešno neutralisao interferenciju anti-CD38 antitela u svim uzorcima pacijenata, omogućavajući pouzdanu detekciju klinički značajnih aloantitela, izuzev anti-Fya i anti-Fyb. Upotrebom reagensa DTT postignuta je potpuna neutralizacija interferencije u sedam od 11 uzoraka.
Zaključak: sCD38 reagens predstavlja efikasnu alternativu DTT reagensu. Očuvanjem eritrocitnih antigena i visokom uspešnošću neutralizacije interferencije, sCD38 reagens značajno unapređuje bezbednost transfuzijskog lečenja pacijenata sa multiplim mijelomom.
Ključne reči: sCD38, daratumumab, DTT, imunohematologija, pretransfuzijsko testiranje, multipli mijelom.

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CONTEMPORARY APPROACHES TO OVERCOMING ANTI-CD38 THERAPY INTERFERENCE IN PRE-TRANSFUSION TESTING: SCD38 OR DTT?

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Introduction: Anti-CD38 monoclonal antibodies, such as daratumumab, are widely used in the treatment of multiple myeloma. By binding to the CD38 antigen expressed on the surface of red blood cells, these agents cause panreactivity in the IAT. Such interference complicates antibody screening, identification of red blood cell alloantibodies, and compatibility testing. Dithiothreitol (DTT) treatment is currently considered the standard method for eliminating this interference.
Objective: To evaluate the significance and effectiveness of the sCD38 reagent in neutralizing anti-CD38 therapy-related interference and to compare its performance with that of DTT in pre-transfusion testing.
Materials and Methods: Serum samples from 11 patients with multiple myeloma receiving daratumumab therapy were analyzed. Interference neutralization was performed using the sCD38 reagent according to the manufacturer's instructions (Grifols, Spain). Subsequently, antibody screening, antibody identification, and compatibility testing were carried out using standard immunohematological methods. The obtained results were compared with those achieved using DTT reagent (BioRad, France).
Results: The sCD38 reagent successfully neutralized anti-CD38 antibody interference in all patient samples, enabling reliable detection of clinically significant alloantibodies, with the exception of anti-Fya and anti-Fyb. Complete neutralization of interference using DTT was achieved in seven out of eleven samples.
Conclusion: The sCD38 reagent represents an effective alternative to DTT in pre-transfusion testing.
Keywords: sCD38, daratumumab, DTT, immunohematology, pre-transfusion testing, multiple myeloma.

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FETALNA I NEONATALNA ALOIMUNA TROMBOCITOPENIJA UZROKOVANA ANTI-HPA-5B ANTITIJELIMA U TRI UZASTOPNE TRUDNOĆE – EFEKAT ANTENATALNE IVIG TERAPIJE

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Uvod: FNAIT - fetalna i neonatalna aloimuna trombocitopenija nastaje usljed majčine aloimunizacije na fetalne trombocitne antigene. Iako su anti-HPA-1a antitijela najčešći uzrok, HPA-5 sistem može biti klinički značajan, ali nedovoljno prepoznat.
Cilj: Prikazati tri uzastopne trudnoće komplikovane FNAIT-om uzrokovanim anti-HPA-5b antitijelima te prikazati neonatalni ishod nakon antenatalne IVIG terapije.
Materijal i metode: Kod pacijentkinje sa ponavljanom neonatalnom trombocitopenijom izvršena je analiza trombocitnih antitijela Luminex metodom i genotipizacija HPA sistema roditelja.Tokom treće trudnoće primijenjena je antenatalna terapija intravenskim imunoglobulinima (IVIG).
Rezultati: Utvrđena je HPA-5 inkompatibilnost (majka HPA-5a/a, otac HPA-5a/b) uz prisustvo anti- HPA-5b antitijela. Prvo dijete imalo je blagu trombocitopeniju bez krvarenja i terapije. Drugo dijete razvilo je tešku trombocitopeniju uz periventrikularno krvarenje I stepena. Primijenjeni su IVIG i jedan trombocitni koncentrat bez prethodne HPA tipizacije; stoga se HPA kompatibilnost trombocitnog koncentrata nije mogla procijeniti.Treće dijete, uz antenatalnu IVIG terapiju, imalo je blažu trombocitopeniju bez transfuzijske potpore i uredan neurosonografski nalaz.
Zaključak: Anti-HPA-5b antitijela mogu uzrokovati rekurentnu FNAIT sa varijabilnom težinom kliničke slike. Ovaj prikaz naglašava značaj rane dijagnostike i HPA genotipizacije, kao i potencijalnu korist antenatalne IVIG terapije u poboljšanju neonatalnog ishoda i smanjenju težine trombocitopenije.
Ključne riječi: fetalna i neonatalna aloimuna trombocitopenija, humani trombocitni antigen (HPA-5), anti- HPA-5b antitijela

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FETAL AND NEONATAL ALLOIMMUNE THROMBOCYTOPENIA CAUSED BY ANTI-HPA-5B ANTIBODIES IN THREE CONSECUTIVE PREGNANCIES - EFFECT OF ANTENATAL IVIG THERAPY

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Introduction: Fetal and neonatal alloimmune thrombocytopenia (FNAIT) is a rare immune-mediated disorder caused by maternal alloantibodies directed against fetal platelet antigens.Although anti -HPA-1a antibodies are most common, the HPA-5 system may also be clinically significant.
Objective: To present three consecutive pregnancies complicated by FNAIT caused by anti -HPA-5b antibodies and to present the neonatal outcome following antenatal intravenosus immunoglobulin (IVIG) therapy.
Materials and methods: Platelet antibody testing was performed using Luminex technology. Parental HPA genotyping was carried out by molecular methods. During the third pregnancy, antenatal IVIG therapy was administered to the mother.
Results: HPA-5 incompatibility was confirmed (mother HPA-5a/a, father HPA-5a/b) with detectable anti-HPA-5b antibodies. The first neonate had mild thrombocytopenia without bleeding or treatment. The second neonate developed severe thrombocytopenia with a grade I periventricular hemorrhage. IVIG and one platelet concentrate were administered without prior HPA typing;therefore, the HPA compatibility of the platelet concentrate could not be assessed. The third neonate, following antenatal IVIG therapy, showed significantly milder thrombocytopenia without transfusion requirement and had normal neurosonographic findings.
Conclusion: Anti-HPA-5b antibodies may cause recurrent FNAIT with variable clinical severity. This case highlights the importance of early immunohematological diagnosis and HPA genotyping, as well as the potential benefit of antenatal IVIG therapy in improving neonatal outcomes.
Keywords: Fetal and Neonatal Alloimmune Thrombocytopenia(FNAIT), Human Platelet Antigen (HPA-5), Anti- HPA-5b antibodies

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SEROLOŠKO – MOLEKULARNA IMUNOHEMATOLOŠKA ANALIZA RETKOG FENOTIPA DAVAOCA KRVI

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Uvod: Jedna od definicija retkog fenotipa glasi da je to odsustvo ekspresije nekoliko antigena istog krvnogrupnog sistema, što se može videti kod Rh sistema. Neke od D-varijanti mogu dati lažno negativan nalaz serološkog testiranja, te je optimalna mogućnost njihovog otkrivanja molekularno testiranje. Cilj: Prikaz značaja integrisanog serološko – molekularnog pristupa u karakterizaciji retkih Rh fenotipova i otkrivanja hibridnih alela u sistemu Rh kod davalaca krvi. Prikaz slučaja: Prikazan je davalac u dobi od 28 godina, koji je prvi put donirao krv 2015. godine, kada je određena krvna grupa O RhD – negativan sa retkim fenotipom CCddee. Od tada je tri puta dobrovoljno donirao krv i svim raspoloživim serološkim metodama (u gelu i epruveti) je potvrđena prethodno određena krvna grupa u ABO i Rh sistemu. Molekularno ispitivanje urađeno je metodom real-time PCR na aparatu FluoQube na Odeljenju za imunohematološka ispitivanja Instituta za transfuziju krvi Srbije. Utvrđeno je da ima deleciju RHD gena. Na lokusu RHCE utvrđeno je postojanje sekvence gena RHD u području 5'UTR (neprevedeni region), što predstavlja hibridni RHCE-RHD alel. Kod davaoca sa tim alelom dokazano je prisustvo D epitopa na eritrocitima metodima adsorpcije i elucije. Na osnovu molekularnog nalaza, utvrđeno prisustvo D epitopa povezano je sa hibridnim RHCE-RHD alelom, a ne sa DEL varijantom RHD gena. Iako ovaj hibridni alel do sada nije zvanično klasifikovan od strane ISBT-a, njegovo postojanje je dokumentovana u dostupnim onlajn bazama podataka za Rh sistem, u kojima su detaljno prikazane i karakteristike njegove genomske strkture. Zaključak: Ovaj prikaz slučaja dodatno potvrđuje značaj integrisanog serološko-molekularnog pristupa u savremenoj transfuzionoj praksi. Pravovremeno prepoznavanje varijanti RHD i RHCE gena omogućava precizniju procenu transfuzionog rizika i predstavlja ključni korak u prevenciji aloimunizacije. Time se direktno unapređuje bezbednost i kvalitet transfuzionog lečenja pacijenta.
Ključne reči: redak fenotip, Rh sistem, molekularno ispitivanje, adsorpcija, elucija, hibridne varijante RHD-RHCE.

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SEROLOGICAL-MOLECULAR IMMUNOHEMATOLOGICAL ANALYSIS OF A RARE BLOOD DONOR PHENOTYPE

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Introduction: One of the definitions of a rare blood group phenotype is the absence of expression of several antigens within a blood group system, as may occur in the Rh blood group system. Certain D variants may yield false - negative serological test results, therefore molecular testing represents the optimal approach for their detection. **Aim:** To demonstrate the importance of an integrated serological and molecular approach in the characterization of rare Rh phenotypes and the detection of hybrid alleles within the Rh blood group system in blood donors. **Case Report:** We present a 28–year-old blood donor who first donated blood in 2015. At that time, he was typed as blood group O, RhD-negative, with rare phenotype CCddee. Since then, he has doneted blood three more times, and all available serological methods (tube and gel techniques) consistently confirmed the previously determined ABO and Rh blood group status. Molecular analysis was performed using real-time PCR on the FluoQube platform at the Department of Immunohematological Testing, Blood Transfusion Institute of Serbia. Deletion of *RHD* gene was identified. Analysis of the *RHCE* locus revealed the presence of an *RHD* gene sequence within the 5' untranslated region (5' UTR), indicating the presence of a hybrid *RHCE-RHD* allele. In donors carrying this allele, the presence of D epitopes on red blood cells has been demonstrated using adsorption and elution techniques. Based on the molecular findings, the detected expression of D epitopes was attributed to the hybrid RHCE-RHD allele rather than to an RHD DEL variant. Although this hybrid allele has not yet been officially classified by the ISBT, its existence has been documented in publicly available online databases dedicated to the Rh blood group system, which also provide detailed information regarding its genomic structure. **Conclusion:** This case report further highlights the significance of an integrated serological – molecular approach in modern transfusion practice. Timely identification of *RHD* and *RHCE* gene variants enables a more accurate assessment of transfusion risk and represents a crucial step in the prevention of alloimmunization, thereby directly improving the safety and quality of transfusion therapy.
Keywords: rare phenotype, Rh blood group system, molecular testing, adsorption, elution, RHCE – RHD hybrid variants;

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DODATNA TESTIRANJA UZORAKA DAVALACA KRVI KOD POZITIVNIH SKRININGA IREGULARNIH ANTITELA

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UVOD: Pravilnikom o kvalitetu u oblasti transfuzijske medicine propisuju se bliži uslovi testiranja krvi i komponenata krvi u ovlašćenim transfuzioloških ustanovama. Davaoci sa klinički značajnim antitelima i sa pozitivnim direktnim Coombsovim testom (DAT) se isključuju iz doniranja krvi.
CILJ RADA: Prikaz i analiza rezultata testiranja skrininga iregularnih antitela i pozitivnog DAT-a kod dobrovoljnih davalaca krvi (DDK) u Institutu za transfuziju krvi Srbije (ITKS).
METODI RADA: Analizirani su podaci za period od 01.01.2020.do 31.12.2025.godine. Skrining iregularnih antitela radi se na automatskim analizatorima. Kod pozitivnih rezultata skrininga antitela, identifikacija antitela obavljala se manuelno metodom u gelu i metodom u epruveti. DAT se radi manuelno metodom u gelu.
REZULTATI: Skrining antitela urađen je za 439351 uzorak dobrovoljnih davalaca krvi, afereznih trombocita i rekonvalescentne Covid plazme. Broj preliminarno pozitivnih skrininga iregularnih antitela je 1458 (0,33%). Od tog broja, nakon ponavljanja i identifikacije, kod 885 DDK skrining iregularnih antitela je negativan (60,7%). Papainska antitela neutvrđene specifičnosti identifikovana su kod 198 DDK (34,5%). Hladna antitela neutvrđene specifičnosti identifikovana su kod 122 DDK (21,2 %). Antitela neutvrdjene specifičnosti identifikovana su kod 30 DDK (5,2%). Klinički značajna antitela su identifikovana kod 223 DDK (38.9 %), anti-D kod 46 DDK (20,6 %), anti-K kod 38 DDK (17 %), anti-E kod 30 DDK (13,4%), anti-c kod 10 DDK (4,5 %), anti-C kod 7 DDK (3,13%), anti-e kod 5 DDK (2,24 %), anti-C^w kod 15 DDK (6,7 %), anti-M kod 29 DDK (13 %). Ostala klinički značajna antitela učestvuju u manjem procentu identifikacija.
Direktni Coombsov test je pozitivan kod 301 DDK (0,07%). Od tog broja samo DAT pozitivnih DDK je 214 (71,1 %), DAT otkriven pri identifikaciji udružen sa nespecifičnim antitelima pozitivan je kod 77 DDK (25.5%), DAT otkriven pri identifikaciji udružen sa klinički značajnim antitelima pozitivan je kod 10 DDK (3,3%).
ZAKLJUČAK: Zbog prisustva klinički značajnih antitela i pozitivnog DAT-a, iz daljeg davanja krvi isključeno je 514 (0,12%) DDK.
Ključne reči: Algoritam, skrining, identifikacija.

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ADDITIONAL TESTING OF BLOOD DONORS IN CASE OF POSITIVE SCREENINGS FOR IRREGULAR ANTIBODIES

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INTRODUCTION: The quality regulations in the field of transfusion medicine prescribes more detailed conditions for testing blood and blood components in authorized transfusion institutions. Donors with clinically significant antibodies and with a positive direct Coombs test (DAT) are excluded from donating blood.
OBJECTIVE OF THE WORK: Presentation and analysis of the results of irregular antibody screening (scr) and positive direct Coombs test (DAT) in voluntary blood donors (VBD) at the Blood Transfusion Institute of Serbia (BTIS).
WORKING METHODS: Data for the period from January 1, 2020 to December 31, 2025 were analyzed. Screening of irregular antibodies was done on automatic analyzers. In the case of positive antibody screening results, antibody identification was performed manually using the gel method and the test tube method. DAT was done manually using the gel method.
RESULTS: Antibody screening was performed for 439351 samples of voluntary donors of blood, apheresis platelets and convalescent Covid plasma. The number of preliminary positive irregular antibody screenings was 1458 (0.33%). After repetition and identification, in 885 VBD screening for irregular antibodies was negative (60.7%). Papain antibodies of undetermined specificity were identified in 198 VBD (34.3%). Cold antibodies of undetermined specificity were identified in 122 VBD (21.3%). Antibodies of undetermined specificity were identified in 30 VBD (5.2 %). Clinically significant antibodies were identified in 223 VBD (38.9%), anti-D in 46 VBD (20.6%), anti-K in 38 VBD (17%), anti-E in 30 VBD (13.4%), anti-c in 10 VBD (4.5%), anti-C in 7 VBD(3.13%), anti-e in 5 VBD (2.24%) anti-C^w in 15 VBD (6,7%), and anti-M in 29 VBD (13%). Other clinically significant antibodies participate in a smaller percentage of identifications. The direct Coombs test was positive in 301 DDK (0.07%). Of that number only DAT-positive DDK was 214 (71.1%), DAT detected during identification associated with non-specific antibodies was positive in 77 DDK (25.5%), DAT detected during identification associated with clinically significant antibodies was positive in 10 DDK (3.3%).
CONCLUSION: Due to the presence of clinically significant antibodies and positive DAT, 514 (0.12%) DDK were excluded from further blood donation.
Keywords: Algorithm, screening, identification.

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PRIPREMA KRVI ZA EKSANGVINO TRANSFUZIJU KOD PACIJENATA ODELJENJA ZA PRETRANSFUZIONA ISPITIVANJA, DISTRIBUCIJU KRVI I PRODUKATA OD KRVI I HEMOVIGILANCU INSTITUTA ZA TRANSFUZIJU KRVI SRBIJE

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Uvod: Eksangvino transfuzija (EST) predstavlja zamenu krvi novorođenčeta kompatibilnom krvlju davaoca. Primenjuje se kod novorodjenčeta sa teškom nekonjugovanom hiperbilirubinemijom radi prevencije kernikterusa. Najčešća indikacija za EST je hemolizna bolest novorođenčeta (HBN).
Cilj: Utvrditi učestalost pripreme krvi za potrebe EST kod pacijenata Odeljenja za pretransfuziona ispitivanja, distribuciju krvi i produkata od krvi i hemovigilancu Instituta za transfuziju krvi Srbije.
Metode: Urađena je retrospektivna analiza podataka iz Protokola Odeljenja i informacionog sistema u periodu 13.03.2022 - 13.06.2026. godine. Krvna grupa (KG) je određivana metodom u gel kartici i epruveti. Direktni Coombsov test (DAT) rađen je metodom u gel kartici. Skrining je rađen metodom u indirektnom Coombsovom testu (IAT) ID DiaCell I-II-III. Interreakcija (IR) je rađena metodom u IAT-u u gel kartici i u epruveti. Primenjene jedinice eritrocita bile su starosti do 5 dana, filtrovane, odgovarajuće krvne grupe i fenotipa, resuspendovane u plazmi krvne grupe AB.
Rezultati: EST je urađena kod 8 bolesnika. Kod 5 novorođenčadi indikacija za EST bila je HBN uzrokovana aloimunizacijom (62,5%). Najčešće identifikovano antitelo kod HBN bilo je anti-c kod 3 pacijenta (60 %) i anti-D kod 2 pacijenta (40%), od kojih je jedno imalo anti-D+E. Sva novorođenčad sa HBN imala su pozitivan DAT polispecifičan i monospecifičan i IAT (3+ do 4+). Kod 3 novorođenčeta (37,5%) indikacija za EST bila je druge etiologije i imala su negativan DAT i IAT.
Zaključak: Pravovremena i precizna imunohematološka priprema krvi je ključna u izvođenju eksangvino transfuzije. Iako je EST danas retka procedura, hemolitička bolest novorođenčeta i dalje ostaje njena vodeća indikacija.
Ključne reči: Eksangvino transfuzija, hemolizna bolest novorođenčeta, direktni Coombsov test, indirektni Coombsov test.

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PREPARATION OF BLOOD COMPONENTS FOR EXCHANGE TRANSFUSION IN PATIENTS TESTED IN THE DEPARTMENT FOR PRETRANSFUSION TESTING, BLOOD AND BLOOD COMPONENTS DISTRIBUTION AND HEMOVIGILANCE IN BLOOD TRANSFUSION INSTITUTE OF SERBIA

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Introduction: Exchange transfusion (ECT) represents the replacement of a newborn's blood with compatible donor blood. It is applied in newborns with severe unconjugated hyperbilirubinemia for the prevention of kernicterus. The most common indication for ECT is hemolytic disease of the fetus and newborn (HDFN).
Aim: The aim of this study was to determine the frequency of blood components preparation for ECT at the Department for Pretransfusion Testing, Blood and Blood Components distribution and Hemovigilance in Blood Transfusion Institute of Serbia.
Methods: A retrospective analysis from the Department's Registry and information system was performed between March 13, 2022 and June 13, 2026. Blood grouping was performed using gel card and conventional tube methods. Direct antiglobulin test (DAT) was performed using gel card method. Antibody screening was performed using indirect antiglobulin test (IAT) ID DiaCell I-II-III. Crossmatching was performed by IAT method using gel card and tube techniques. Transfused red blood cell units were up to 5 days old, leukoreduced, matched for blood group and phenotype and resuspended in AB plasma.
Results: ECT was performed in 8 patients. In 5 newborns, the indication for ECT was HDFN caused by alloimmunization (62.5%). The most common antibody causing HDFN was anti-c detected in 3 patients (60%) and anti-D detected in 2 patients (40%), one of whom had anti-D+E. All newborns with HDFN had a positive polyspecific and monospecific DAT and IAT (3+ to 4+). In 3 newborns (37.5%), the indication for ECT was of a different etiology with negative DAT and IAT.
Conclusion: Timely and accurate immunohematological preparation of blood components is crucial for successful exchange transfusion. Although ECT is a rare procedure today, HDFN remains its leading indication.
Key words: Exchange transfusion, hemolytic disease of the fetus and newborn, direct antiglobulin test, indirect antiglobulin test.

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ANTITHROMBIN: CONTEMPORARY GUIDELINES AND FUTURE PERSPECTIVE

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Antithrombin (AT) is a key natural anticoagulant, structurally an alpha-2 glycoprotein from the serpin superfamily that is synthesized in the liver, and acts by inhibiting primarily thrombin (FII), F Xa, but also FIXa, FXIa, and FXIIa, as a tissue factor-FVIIa complex. People with a hereditary form of AT deficiency have a 15 times higher risk of developing venous thrombosis, with a note that in certain subtypes there is an increased risk of arterial thrombosis.

It is estimated that people with a hereditary form of AT deficiency have a 15 times higher risk of developing venous thrombosis and a risk that 50% will develop thrombosis by the age of 50, and 85% by the end of life. The rate of recurrent venous thromboembolism in patients with AT deficiency is significantly higher, so this condition is considered a high-risk thrombophilia. The risk of thrombosis in people with antithrombin deficiency is particularly pronounced during pregnancy and puerperium, sepsis, trauma, major surgical interventions, certain procedures and requires special consideration in the prevention of thromboembolic complications.

The most common acquired causes of AT deficiency are nephrotic syndrome, sepsis, liver diseases, enteropathies with malnutrition, disseminated intravascular coagulation (DIC), microangiopathic hemolytic anemia, veno-occlusive disease in patients who have undergone bone marrow transplantation, noting that major surgical interventions, massive transfusions, use of equipment for intraoperative blood saving and dialysis procedures, ECMO (Extracorporeal Membrane Oxygenation) preeclampsia and eclampsia, the use of oral contraceptives and heparin preparations are conditions that are significantly associated with antithrombin deficiency.

Antithrombin deficiency is associated with therapeutic resistance to the action of unfractionated heparin, low molecular weight heparin and fondaparinux.

Pleiotropic properties of AT such as anti-inflammatory, immunomodulatory, antiangiogenic and antiplatelet properties indicate significant potential in the treatment of various pathological processes such as sepsis-induced DIC, but there is no agreement for use in these indications in most international recommendations. Timely detection of AT deficiency, as well as appropriate treatment of pathological conditions caused by antithrombin deficiency, especially in the prophylaxis and therapy of thromboembolism, are of crucial importance for a positive outcome of the disease.

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REVERZIJA DEJSTVA DABIGATRANA PRIMENOM IDARUCIZUMABA I HEMODIJALIZE KOD PACIJENTA SA RUPTUROM ANEURIZME ABDOMINALNE AORTE

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Uvod: Dabigatran je direktni oralni antikoagulans koji se koristi u prevenciji i lečenju tromboembolijskih oboljenja. U slučajevima životno ugrožavajućeg krvarenja, koje zahteva hitnu hiruršku intervenciju, brza reverzija antikoagulantnog efekta je od ključnog značaja. Idarucizumab je specifični antidot za dabigatran, dok hemodijaliza može dodatno da pospeši eliminaciju leka, naročito kod pacijenata sa oštećenom bubrežnom funkcijom.

Cilj: Prikaz zbrinjavanja pacijenta na terapiji dabigatranom, kod koga je došlo do rupture aneurizme abdominalne aorte, što je zahtevalo hitnu hiruršku intervenciju i reverziju antikoagulantnog dejstva.

Materijal i metode: Prikazujemo slučaj 70-godišnjeg muškarca na hroničnoj terapiji dabigatranom, koji je operisan zbog rupture aneurizme abdominalne aorte i hemoragijskog šoka. Zbog hitnosti procedure, koagulacioni status i bubrežna funkcija procenjeni su naknadno tokom operacije. Efekat dabigatrana praćen je Ecarin Clotting Assay testom (ClotPro), a njegova reverzija postignuta je intravenskom primenom idarucizumaba i hemodijalizom. Zbog sumnje na perzistentnu antikoagulantnu aktivnost i smanjeno neutralisanje leka, nakon hitne hirurške rekonstrukcije sprovedene su pored primene idarucizumaba i dve uzastopne hemodijalize u razmaku od 24 sata. Analizirani su klinički, laboratorijski i perioperativni ishodi.

Rezultati: Idarucizumab je brzo neutralisao antikoagulantni efekat dabigatrana, ali njegov povratni efekat, zahtevao je primenu hemodijaliza, koje su dodatno doprinele smanjenju koncentracije dabigatrana u cirkulaciji. Hemodijaliza je neophodna kod pacijenata sa ekstremnim predoziranjem, kako bi se smanjila aktivnost leka u krvotoku. Kod pacijenta je postignuta uredna hemostaza bez trombotičkih komplikacija povezanih sa reverzijom antikoagulantne terapije.

Zaključak: Kombinacija idarucizumaba i hemodijalize može obezbediti efikasnu reverziju dejstva dabigatrana kod kritično obolelih pacijenata, kojima je potrebna hitna hirurška intervencija. Ovakav pristup može poboljšati kliničke ishode u situacijama kada je neophodna brza i potpuna reverzija antikoagulacije uz adekvatno praćenje antikoagulantnog efekta brzim point of care (ECAT) testom.

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DABIGATRAN REVERSAL USING IDARUCIZUMAB AND HEMODIALYSIS IN A PATIENT WITH RUPTURED ABDOMINAL AORTIC ANEURYSM

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Background: Dabigatran is a direct oral anticoagulant increasingly used for the prevention and treatment of thromboembolic diseases. In cases of life-threatening bleeding requiring emergency surgery, rapid reversal of anticoagulation is critical. Idarucizumab is a specific antidote for dabigatran, while hemodialysis can further enhance drug elimination, particularly in patients with impaired renal function.

Goal: To present the management of a patient receiving dabigatran therapy who developed a ruptured abdominal aortic aneurysm requiring urgent surgical intervention and anticoagulation reversal.

Materials and Methods: We report the case of a 70-year-old male on chronic dabigatran therapy who presented with a ruptured abdominal aortic aneurysm and hemorrhagic shock. Upon admission, coagulation status and renal function were assessed later during surgery due to emergency of a procedure. Dabigatran effect was monitored by Ecarine Clotting Assay test (Clotpro) and its reversal was achieved with intravenous idarucizumab and hemodialysis. Due to concerns regarding persistent anticoagulant activity and/or impaired drug clearance, two hemodialysis were performed after emergency surgical repair. Clinical, laboratory, and perioperative outcomes were analyzed.

Results: Idarucizumab rapidly neutralized the anticoagulant effect of dabigatran. Hemodialysis contributed to further reduction of circulating dabigatran levels and is necessary in extremly overdosed patient in order to decrease the activity of drug in bloodstream. The patient achieved normal hemostasis without reversal-related thrombotic complications.

Conclusion: The combination of idarucizumab and hemodialysis can provide effective dabigatran reversal in critically ill patients with emergency surgical interventions. This approach may improve clinical outcomes in situations where rapid and complete anticoagulation reversal is required with adequate monitoring of anticoagulation.

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UTICAJ LABORATORIJSKIH METODA NA DIJAGNOSTIKU DEFICITA ANTITROMBINA U PERIODU 1997-2025

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Deficit antitrombina (AT) je najznačajnija urođena trombofilija koja se nasleđuje autozomno dominantno. Dijagnostika se zasniva na koagulacionim metodama za procenu funkcionalne aktivnosti AT, imunološkim metodama za određivanje antigena i genetičkoj analizi. Tokom poslednjih 30 godina korišćeni su različiti funkcionalni testovi zasnovani na inhibiciji faktora IIa ili Xa u prisustvu heparina. Test heparin kofaktor aktivnosti, koji je snižen kod svih tipova deficita, prihvaćen je kao prva linija dijagnoze. Kod osoba sa sniženim AT važno je utvrditi tip mutacije (I ili II) i da li ona utiče na vezivanje heparina, reaktivno mesto ili ima pleotropni efekat.

Cilj rada bio je hronološki prikaz testiranja na trombofilije uz osvrt na uvođenje metoda za detekciju deficita AT. Retrospektivno su analizirani podaci od januara 1997. do decembra 2025. o broju testiranja, korišćenim metodama i registrovanim deficitima. Za određivanje aktivnosti AT korišćeni su reagensi HemosIL (koagulometar ACL7000), AT Berichrom i AT Innovance (koagulometar BCS XP Siemens).

U posmatranom periodu testirano je 11.257 bolesnika. Od 1997–2011. korišćen je reagens HemosIL, ispitano 4343 bolesnika, otkriveno 9 deficita (0,2%). Od 2011–2017. primenjivan je AT Berichrom, otkriveno 14 deficita od 2647 ispitanih (0,53%). Od 2017. uveden je AT Innovance, registrovano 106 deficita (2,48%) od 4267 ispitanih. Implementacija novih metoda povećala je detekciju deficita sa 0,2% na 2,48%.

Zaključak: Unapređenje laboratorijskih metoda značajno je poboljšalo dijagnostiku deficita AT, što je dovelo do većeg broja novootkrivenih pacijenata. Svi deficiti otkriveni AT Innovance reagensom potvrđeni su genetičkim testiranjem, što naglašava važnost odabira dovoljno senzitivanog testa.

Kljucne reči:AT deficit,metode testiranja,hromogeni testovi

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IMPACT OF LABORATORY METHODS ON THE DIAGNOSIS OF ANTITHROMBINDEFICIENCY,1997-2025

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Antithrombin (AT) deficiency is the most clinically significant inherited thrombophilia, transmitted in an autosomal dominant manner. Diagnostic approaches rely on coagulation assays to assess AT functional activity, immunological methods for antigen quantification, and genetic analysis. Over the past three decades, various functional assays based on inhibition of factor IIa or Xa in the presence of heparin have been employed. The heparin cofactor activity assay, which is reduced in all types of AT deficiency, has been established as the first-line diagnostic test. In patients with reduced AT activity, it is essential to determine the mutation type (I or II) and whether it affects heparin binding, the reactive site, or has a pleiotropic effect.

The aim of this study was to provide a chronological overview of thrombophilia testing, with emphasis on the introduction of methods for detecting AT deficiency. Retrospective data from January 1997 to December 2025 were analyzed, including the number of tests performed, methods applied, and deficiencies identified. AT activity was determined using HemosIL reagents (ACL7000 coagulometer), AT Berichrom, and AT Innovance (BCS XP Siemens coagulometer).

During the study period, 11257 patients were tested. From 1997–2011, HemosIL reagent was used, with 4343 patients tested and 9 deficiencies identified (0.2%). Between 2011–2017, AT Berichrom was applied, detecting 14 deficiencies among 2647 patients (0.53%). Since 2017, AT Innovance has been introduced, with 106 deficiencies identified (2.48%) among 4267 patients. The implementation of newer methods increased detection rates from 0.2% to 2.48%.

Conclusion: Advances in laboratory methods have significantly improved the diagnosis of AT deficiency, resulting in a higher number of newly identified patients. All deficiencies detected with the AT Innovance reagent were confirmed by genetic testing, underscoring the importance of selecting sufficiently sensitive assays.

Keywords: Antithrombin deficiency, diagnostic methods, chromogenic assays

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TRETMAN HEPARINOM INDUKOVANE TROMBOCITOPENIJE TIP II PRIMENOM FONDAPARINUX-A I TERAPIJSKIM IZMENAMA PLAZME UZ MONITORING POINT OF CARE RUSSELL VIPER VENOM TESTOM

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Uvod: Heparinom indukovana trombocitopenija tip II (HIT II) predstavlja ozbiljnu imunološki posredovanu komplikaciju primene heparina, karakterisanu trombocitopenijom i povećanim rizikom od arterijskih i venskih tromboza. Pravovremeno prepoznavanje i uvođenje alternativne antikoagulantne terapije od ključnog su značaja za smanjenje morbiditeta i mortaliteta.

Cilj: Prikaz uspešnog postoperativnog lečenja bolesnika sa HIT tip II primenom fondaparinuksa, terapijskim izmenama plazme (TIP) uz monitoring koagulacionog statusa Point-of-Care Russel Viper Venom testom (RVVT) – ClotPro.

Materijali i metode: Prikazan je slučaj pacijentkinje starosti 64 godine sa klinički i laboratorijski potvrđenim HIT tip II, kod koje je nakon obustavljanja heparina uveden fondaparinuks. Pacijentkinji je operisana aneurizma torakoabdominalne aorte sa ezofagealnom fistulom koristeći bovin graft. Posle operacije pacijentkinja ulazi u dijalizno zavisnu akutnu bubrežnu insuficijenciju. Zbog trombocitopenije i potvrđenih HIT antitela i započeto lečenje fondaprinuksom uz dve uzastopne TIP. Efikasnost TIP i antikoagulantne terapije praćene su Point-of-Care RVV testom (ClotPro), uz redovno određivanje broja trombocita i standardnim koagulacionim laboratorijskim testovima.

Rezultati: Nakon primene TIP i terapije fondaparinuksom zabeležen je postepen porast broja trombocita i stabilizacija kliničkog stanja. Terapijske izmene plazme dovele su do smanjenja aktivnosti patogenih antitela i dodatnog poboljšanja laboratorijskih parametara. Monitoring Point-of-Care RVV testom omogućio je brzu procenu antikoagulantnog efekta i bezbedno prilagođavanje terapije. Tokom lečenja nisu registrovane nove trombotične komplikacije niti značajna krvarenja.

Zaključak: Kombinovana primena fondaparinuksa i terapijskih izmena plazme može predstavljati efikasan terapijski pristup kod bolesnika sa HIT II visokog rizika. Point-of-Care RVVT monitoring omogućava pravovremenu procenu antikoagulantnog efekta i može doprineti bezbednijem vođenju terapije u ovoj kompleksnoj kliničkoj situaciji.

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TREATMENT OF HEPARIN-INDUCED THROMBOCYTOPENIA TYPE II WITH FONDAPARINUX AND THERAPEUTIC PLASMA EXCHANGE MONITORED BY POINT-OF-CARE RUSSELL VIPER VENOM TEST

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Introduction: Heparin-induced thrombocytopenia type II (HIT II) is a serious immune-mediated complication of heparin therapy, characterized by thrombocytopenia and an increased risk of arterial and venous thrombosis. Early recognition and prompt initiation of alternative anticoagulant therapy are crucial for reducing morbidity and mortality.

Objective: To present the successful postoperative management of a patient with HIT type II using fondaparinux and therapeutic plasma exchange (TPE), with coagulation status monitored by a Point-of-Care Russell Viper Venom Test (RVVT) using the ClotPro system.

Materials and Methods: We report the case of a 64-year-old female patient with clinically and laboratory-confirmed HIT type II. Following discontinuation of heparin, anticoagulant therapy with fondaparinux was initiated. The patient underwent surgery for a thoracoabdominal aortic aneurysm complicated by an esophageal fistula, using a bovine graft. Postoperatively, she developed dialysis-dependent acute kidney injury. Due to thrombocytopenia and confirmed HIT antibodies, treatment with fondaparinux was initiated along with two consecutive sessions of therapeutic plasma exchange (TPE). The effectiveness of TPE and anticoagulant therapy was monitored using the Point-of-Care RVVT (ClotPro), together with regular platelet count measurements and standard coagulation laboratory tests.

Results: Following TPE and fondaparinux therapy, a gradual increase in platelet count and stabilization of the patient's clinical condition were observed. Therapeutic plasma exchange resulted in reduced activity of pathogenic antibodies and further improvement in laboratory parameters. Point-of-Care RVVT monitoring enabled rapid assessment of the anticoagulant effect and safe adjustment of therapy. No new thrombotic complications or significant bleeding events were recorded during treatment.

Conclusion: The combined use of fondaparinux and therapeutic plasma exchange may represent an effective treatment strategy for high-risk patients with HIT II. Point-of-Care RVVT monitoring allows timely assessment of anticoagulant activity and may contribute to safer management of therapy in this complex clinical setting.

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PROMENE U PERIOPERATIVNOM UTROŠKU KRVNIH PRODUKATA NAKON UVOĐENJA ALGORITMA ZA ZBRINJAVANJE MASIVNOG KRVARENJA VOĐENOG VISKOELASTIČNIM TESTOVIMA – ISKUSTVO JEDNOG CENTRA

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Uvod: Perioperativno masivno krvarenje predstavlja najčešći razlog veće primene krvi i krvnih produkata kod hirurških bolesnika. Savremeni pristup zbrinjavanju perioperativne koagulopatije uključuju ciljanu transfuzijsku strategiju zasnovanu na rezultatima viskoelastičnih testova hemostaze, sa ciljem racionalnije primene krvnih produkata. U našoj ustanovi algoritam za zbrinjavanje masivnog perioperativnog krvarenja vođen viskoelastičnim testovima uveden je 2016. godine. **Cilj:** Analiza promena u obimu i strukturi perioperativnog utroška krvnih produkata pre i nakon uvođenja algoritma za zbrinjavanje masivnog krvarenja vođenog viskoelastičnim testovima hemostaze. **Metode:** Sprovedena je retrospektivna analiza godišnjeg utroška koncentrovanih eritrocita (KE), zamrznute sveže plazme (ZSP), krioprecipitata i koncentrovanih trombocita (KT) u Klinici za anesteziju i intenzivno lečenje VMA u periodu od 2010. do 2022. godine. Posmatrani period podeljen je na interval pre uvođenja algoritma (2010–2015) i interval nakon njegovog uvođenja (2016–2022). Razlike između dva perioda analizirane su Mann–Whitney U testom. **Rezultati:** Nakon uvođenja algoritma zabeležen je statistički značajno manji godišnji utrošak ZSP (3.012 ± 509 naspram 1.314 ± 134 jedinica; –56,4%; p = 0,001), uz istovremeno veći utrošak krioprecipitata (954 ± 279 naspram 1.314 ± 233 jedinica; +37,7%; p = 0,005). Odnos ZSP:krioprecipitat promenjen je sa 3,2:1 na 1,0:1, što može ukazivati na promenu obrazaca transfuzijske podrške ka selektivnijoj nadoknadi fibrinogena. Uočen je trend smanjenja godišnjeg utroška KE (1.349 ± 204 naspram 1.114 ± 97 jedinica; –17,4%; p = 0,052), dok smanjenje utroška KT (–19,6%) nije dostiglo statističku značajnost. **Zaključak:** Uvođenje algoritma za zbrinjavanje masivnog perioperativnog krvarenja vođenog viskoelastičnim testovima bilo je udruženo sa promenama u obrascima primene krvnih produkata, pre svega smanjenjem utroška ZSP i većom upotrebom krioprecipitata. Nalazi mogu ukazivati na racionalizaciju transfuzijske prakse i selektivniji pristup korekciji poremećaja hemostaze, ali ih treba tumačiti u kontekstu retrospektivnog, opservacionog dizajna i mogućih vremenski uslovljenih promena u kliničkoj praksi.
Ključne reči: krvni produkti, perioperativna transfuzija, algoritam zbrinjavanja krvarenja, viskoelastični testovi hemostaze

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CHANGES IN PERIOPERATIVE BLOOD PRODUCT UTILIZATION FOLLOWING IMPLEMENTATION OF A VISCOELASTIC TEST GUIDED MASSIVE HEMORRHAGE ALGORITHM – A SINGLE-CENTER EXPERIENCE

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Introduction: Massive perioperative hemorrhage is the most common reason for increased use of blood and blood products in surgical patients. Contemporary management of perioperative coagulopathy incorporates a targeted transfusion strategy based on viscoelastic hemostasis testing, with the aim of rationalizing blood product use. In our institution, a viscoelastic test-guided algorithm for massive perioperative hemorrhage management was implemented in 2016. **Objective:** To analyze changes in the volume and composition of perioperative blood product utilization before and after the implementation of a viscoelastic test-guided massive hemorrhage algorithm. **Methods:** A retrospective analysis of annual consumption of red blood cell concentrates (RBC), fresh frozen plasma (FFP), cryoprecipitate, and platelet concentrates (PC) at the Clinic for Anaesthesia and Intensive Care, MMA, was performed for the period 2010–2022. The observation period was divided into a pre-algorithm interval (2010–2015) and a post-algorithm interval (2016–2022). Differences between the two periods were analyzed using the Mann–Whitney U test. **Results:** Following algorithm implementation, a statistically significant reduction in annual FFP consumption was observed (3,012 ± 509 vs. 1,314 ± 134 units; –56.4%; p = 0.001), along with a significant increase in cryoprecipitate use (954 ± 279 vs. 1,314 ± 233 units; +37.7%; p = 0.005). The FFP-to-cryoprecipitate ratio changed from 3.2:1 to 1.0:1, suggesting a shift in transfusion support patterns toward more selective fibrinogen replacement. A trend toward reduced annual RBC consumption was observed (1,349 ± 204 vs. 1,114 ± 97 units; –17.4%; p = 0.052), while the reduction in platelet concentrate use (–19.6%) did not reach statistical significance. **Conclusion:** Implementation of a viscoelastic test-guided massive hemorrhage algorithm was associated with changes in blood product utilization patterns, primarily a reduction in FFP consumption and increased use of cryoprecipitate. These findings may suggest a rationalization of transfusion practice and a more selective approach to hemostasis correction, but should be interpreted in the context of the retrospective, observational study design and potential time-related changes in clinical practice.
Keywords: blood products, perioperative transfusion, hemorrhage management algorithm, viscoelastic hemostasis testing

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REZULTATI UČEŠĆA U SPOLJAŠNJIM KONTROLAMA ZA ISPITIVANJE TESTOVA TROMBOFILIJE U PERIODU 2021-2025. GODINE

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Uvod: Trombofilija predstavlja poremećaj koagulacije u smislu povećane sklonosti ka zgrušavanju krvi koje se najčešće ispoljava kao tromboza, plućna embolija ili spontani pobačaj. U laboratorijskom ispitivanju trombofilija neophodno je da se dobiju pouzdani rezultati na osnovu kojih se procenjuje rizik za trombozu i odlučuje o uvođenju i trajanju profilakse ili lečenja. Učešće u UKNEQAS spoljašnjim kontrolama omogućava objektivnu procenu kvaliteta rada laboratorije i upoređivanje rezultata na međunarodnom nivou. **Cilj:** Prikaz rezultata spoljašnjih kontrola UKNEQAS za trombofilije koje su urađene na Odeljenju za ispitivanje poremećaja hemostaze **Materijal i metode:** U periodu od 2021. do 2025. godine u okviru programa UKNEQAS Coagulation iz Sheffield-a ispitano je 115 uzoraka plazme. Od toga, 80 uzoraka trombofilija (antitrombin (AT), protein C (PC), slobodni antigen proteina S (Free PSAg) i rezistencija na aktivirani protein C (APC-R)), 16 uzoraka lupus antikoagulansa (LA) - LA screen i LA confirm i 19 uzoraka D-dimera. Uzorci su dobijeni u liofilizovanom obliku i pripremljeni su za ispitivanje na Odeljenju. Analize su urađene na koagulometru Siemens BCS-XP. Dobijeni rezultati su od strane organizatora upoređivani sa rezultatima drugih učesnika i predstavljeni preko Z-skora i performanse laboratorije. **Rezultati:** Od ispitanih uzoraka trombofilija 71 (89%) je bilo u konsenzusu,a 9 (11%) je bilo van konsenzusa (6 PC i 3 Free PSAg). Svi rezultati lupus antikoagulansa su bili u konsenzusu. Od rezultata D-dimera 17 (89.5%) je bilo u konsenzusu, a 2 (10.5%) je bilo van konsenzusa. Vrednosti Z-scora su se kretale u granicama, osim 1 rezultata PC i 1 rezultata D-dimera. Svi rezultati van granica Z-skora i van konsenzusa su bili prihvatljivi. Značajno je takođe da su dijagnostikovani svi patološki uzorci. **Zaključak:** Dobijeni rezultati ukazuju da je ukupna performansa laboratorije u ispitivanju trombofilije vrlo dobra, što je važno za unapređenje kvaliteta rada, pouzdanost laboratorijskih nalaza i poverenja u laboratoriju.
Ključne reči: spoljašnja, kvalitet, kontrola, trombofilije

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RESULTS FROM EXTERNAL QUALITY ASSESSMENT SCHEME FOR THROMBOPHILIA TESTING FROM 2021 TO 2025

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Introduction: Thrombophilia is a coagulopathy characterized by an increased tendency for blood clot formation, most commonly manifested as thrombosis, pulmonary embolism, or recurrent spontaneous miscarriage. In laboratory testing for thrombophilia, reliable results are essential for assessing thrombosis risk and deciding on the initiation and duration of prophylaxis or treatment. Participation in UK NEQAS Coagulation External Quality Assessment Scheme enables objective evaluation of laboratory performance and international comparison of results. **Aim:** To present the results of the UK NEQAS External Quality Assessment Scheme for thrombophilia testing performed at the Haemostasis Department**. Material and Methods:** From 2021 to 2025, within the UK NEQAS Coagulation, 115 plasma samples were analyzed. These included 80 thrombophilia samples (antithrombin (AT), protein C (PC), free protein S antigen (Free PSAg), and activated protein C resistance (APC-R)), 16 lupus anticoagulant (LA) samples – LA screen and LA confirm, and 19 D-dimer samples. The samples were provided in lyophilized form and prepared for testing at the Department. Analyses were performed using the Siemens BCS-XP coagulation analyzer. The obtained results were compared by the organizer with those of other participants and presented through Z-scores and laboratory performance evaluation. **Results:** Among the analyzed thrombophilia samples, 71 (89%) were within consensus, while 9 (11%) were out of consensus (6 PC and 3 Free PSAg results). All lupus anticoagulant results were within consensus. Among the D-dimer results, 17 (89.5%) were within consensus, while 2 (10.5%) were out of consensus. Z-score values were within acceptable limits except for 1 PC result and 1 D-dimer result. All results outside the Z-score limits and outwith consensus were considered acceptable. Importantly, all pathological samples were identified. **Conclusion:** The obtained results indicate that the overall laboratory performance in thrombophilia testing is very good, which is important for improving quality, ensuring reliability of laboratory findings and maintaining confidence in the laboratory.
Key words: external, quality, control, thrombophilia

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NAT SKRINING DOBROVOLJNIH DAVALACA KRVI U INSTITUTU ZA TRANSFUZIOLOGIJU I HEMOBIOLOGIJU VMA: 20 GODINA ISKUSTVA I DOPRINOSA BEZBEDNOSTI TRANSFUZIJE

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Ciljevi: Prikaz razvoja testiranja NAT (Nucleic Acid Testing) metodom uzoraka dobrovoljnih davalaca krvi u Institutu za transfuziologiju i hematologiju VMA od pula od 24 uzorka do pojedinačnog testiranja.
Metode: Testiranje davalaca krvi je započeto 2007. godine na poluautomatizovanom sistemu Roche COBAS Amplicor/COBAS Ampliprep u pulu od 24 uzorka. Automatizovani sistem Roche S201 je uveden 2012. godine, takođe u pulu od 24 uzorka, dok je Grifols Procleix Panter uveden 2022. godine za testiranje pojedinačnih uzoraka.
Rezultati: Tokom perioda od 2007.–2019. godine, 70.938 dobrovoljnih davalaca krvi je testirano u pulu od 24. uzorka, na virus humane imunodeficijencije, hepatitis tipa B i C, a od 2022. godine 63.674 davalaca je testirano pojedinačno na ove uzročnike hematogenih transmisivnih bolesti.
Zaključak: Institut za transfuziologiju i hemobiologiju se od svog osnivanja 1950. godine, trudio da hospitalizovanim pacijentima obezbedi maksimalno sigurnu krv i produkte od krvi. Uvođenje i dvodecenijsko testiranje uzoraka dobrovoljnih davalaca krvi NAT metodom, kako u pulu od 24 uzorka, tako i pojedinačno je nastavak ove tradicije.

Ključne reči: NAT metoda, dobrovoljni davaoci krvi, testiranje.

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NAT SCREENING OF VOLUNTARY BLOOD DONORS AT THE INSTITUTE OF TRANSFUSIOLOGY AND HEMOBIOLOGY OF MMA: 20 YEARS OF EXPERIENCE AND CONTRIBUTION TO TRANSFUSION SAFETY

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Goals: Presentation of the development of NAT (Nucleic Acid Testing) method for testing voluntary blood donor samples at the Institute of Transfusiology and Hemobiology of the MMA from a mini pool (MP) of 24 samples to individual testing (ID).

Methods: Testing began in 2007. on the semi-automated COBAS Amplicor/ COBAS Ampliprep system in a pool of 24 samples. The S201 automated system was introduced in 2012, also in a pool of 24 samples, while the Grifols Procleix Panther was introduced in 2022. for testing individual samples.
Results: During the period 2007–2019, a total of 70,938 voluntary blood donors were tested in pools of 24 samples for human immunodeficiency virus (HIV) and hepatitis B and C viruses. Since 2022, 63,674 donors have been tested individually for these transfusion-transmissible infectious agents.
Conclusion: Since its establishment in 1950, the Institute of Transfusiology and Hemobiology has been committed to providing hospitalized patients with the safest possible blood and blood products. The introduction of NAT testing and its continuous implementation over the past two decades, both in pools of 24 samples and on individual donor samples, represents a continuation of this longstanding commitment to blood safety.

Key words: NAT method, voluntary blood donors, testing.

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ZNAČAJ NAT SKRININGA U OTKRIVANJU OKULTNOG HEPATITISA B I RANIH HBV,HCV I HIV INFEKCIJA KOD DOBROVOLJNIH DAVALACA KRVI

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UVOD: NAT - Nucleic acid Amplification Testing predstavlja vaznu dopunu serološkom skriningu dobrovoljnih davalaca krvi (DDK), koja omogućava ranije otkrivanje infekcija transfuzijom prenosivih virusnih oboljenja u periodu seroloskog prozora (WP) , kao i otkrivanje okultne HBV infekcije(OBI).**CILJ:** Prikazati rezultate NAT testiranja DDK iz 7 centara u Republici Srbiji. Osim uzoraka iz Instituta za transfuziju krvi Srbije (ITKS), podaci o serološkim testiranjima su dobijeni iz centara.
METODE: Retrospektivna studija obuhvata ispitivanje 1 467 546 jedinica na prisustvo HBV, HCV, HIV molekularnom metodom, na aparatima Cobas 6800/8800, u minipulu od 6 uzoraka, u periodu jul 2019 –maj 2026.
REZULTATI: Od ukupnog broja, 504 024(34.34%) se odnosi na uzorke ITKS-a. U Srbiji je otkriveno 419(0.0286%) hepatitis B virus (HBV) NAT pozitivnih jedinica. 104/419 (24.82%) je bilo „samo NAT“ pozitivno, a 315/419 (75.17%) su pozitivni “ NAT i serološki”. 200(47.73%) HBV NAT pozitivnih uzoraka su bili iz ITKS-a, od čega je 152(76%) ” NAT i serološki pozitivno”, a 48(24%) “ samo NAT” pozitivno. 46/48 je bilo anti HBc reaktivno (95.83%)- OBI, a 2/48 (4.16%) anti HBc nereaktivne. 144(0.0098%) su hepatitis C virus (HCV) NAT pozitivni. 2 /144(1.38%) su „samo NAT“ pozitivne, a 142/144(98.61%) su pozitivne sa obe metode. Od 58(0.0039%) pozitivnih na prisustvo HIV NAT , 56(96.55%) je pokazalo pozitivnost serološkim i NAT testiranjem,a 2/58(3.44%) „ samo NAT“.
ZAKLJUČAK: Dobijeni rezultati ukazuju na opravdanost NAT testiranja jedinica DDK, jer omogućavaju otkrivanje infekcija u periodu pre pojave seroloških markera i identifikaciju OBI(95.83%).
Ključne reči: NAT- Nucleic acid Amplification Testing, minipool

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THE SIGNIFICANCE OF NAT SCREENING IN THE DETECTION OF OCCULT HEPATITIS B AND EARLY HBV, HCV AND HIV INFECTIONS IN VOLUNTARY BLOOD DONORS

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INTRODUCTION: NAT - Nucleic acid Amplification Testing represents an important supplement to the serological screening of voluntary non –remunerated blood donors (VNRBDs), which enables earlier detection of infections by transfusion of transmissible viral diseases in the period of the serological window (WP), as well as the detection of occult HBV infection (OBI). OBJECTIVE: To present the results of NAT testing of VNRBDs from 7 centers in the Republic of Serbia. Apart from the samples from the Blood Transfusion Institute of Serbia (BTIS), data on serological testing were obtained from the centers. METHODS: The retrospective study includes the examination of 1,467,546 units for the presence of HBV, HCV, HIV by molecular method, on Cobas 6800/8800 devices, in a minipool of 6 samples, in the period July 2019 - May 2026. RESULTS: Of the total number, 504,024 (34.34%) refer to BTIS samples. In Serbia, 419 (0.0286%) hepatitis B virus (HBV) NAT positive units were detected. 104/419 (24.82%) were “only NAT” positive, and 315/419 (75.17%) were “NAT and serology” positive. 200 (47.73%) HBV NAT positive samples were from ITKS, of which 152 (76%) were “NAT and serologically positive”, and 48 (24%) were “only NAT” positive. 46/48 were anti HBc reactive (95.83%) - OBI, and 2/48 (4.16%) were anti HBc non-reactive. 144 (0.0098%) are hepatitis C virus (HCV) NAT positive. 2/144(1.38%) are “only NAT” positive, and 142/144(98.61%) are positive with both methods. Of the 58 (0.0039%) positive for the presence of HIV NAT, 56 (96.55%) showed positivity by serological and NAT testing, and 2/58 (3.44%) “only NAT”.
CONCLUSION: The obtained results indicate the justification of NAT testing of VNRBDs units, because they enable the detection of infections in the period before the appearance of serological markers and the identification of OBI (95.83%).
Keywords: NAT- Nucleic acid Amplification Testing, minipool

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SIFILIS KOD DOBROVOLJNIH DAVALACA KRVI- REZULTATI INSTITUTA ZA TRANSFUZIJU KRVI SRBIJE

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Uvod: Sifilis predstavlja značajan javnozdravstveni problem uprkos dostupnosti dijagnostike i terapije. Transfuzijske službe imaju važnu ulogu u prevenciji transmisije infekcije putem krvi, kroz obavezni skrining svih jedinica krvi na *Treponema pallidum.* **Cilj rada:** Prikaz i analiza učestalosti pozitivnih rezultata potvrdnog testiranja na sifilis u populaciji dobrovoljnih davalaca krvi u Institutu za transfuziju krvi Srbije. **Materijal i metode:** Sprovedena je retrospektivna analiza rezultata testiranja na sifilis obavljenih kod 420 098 davalaca krvi, u periodu 2020-2025. Sva testiranja su obavljena pod istim uslovima korišćenjem automatizovanih platformi primenom ELISA i CMIA testova. Kod davalaca sa ponovo reaktivnim rezultatima skrining testa, prema nacionalnom algoritmu testiranja, sprovodeno je potvrdno testiranje imunoblot testovima. **Rezultati:** Pozitivan potvdni test je dobijen kod 174 davaoca (0,041 %) od čega je 154 (88,5 %) davaoca muškog pola, a 20 (11,5 %) ženskog pola. 94 (54 %) potvrdjeno pozitivnih rezultata je detektovano kod davalaca koji su krv donirali prvi put, a preostalih 80 (46 %) kod višestrukih davalaca. Potvrdjeno pozitivni rezultati su najzastupljeniji u starosnoj grupi od 31-40 godina, kod 54 davaoca (31,03 %). Kod tri davaoca prisutna je pridružena infekcija (HIV i HBV). Svi potvrdjeno pozitivni davaoci su pozvani u Savetovalište za davaoce krvi, a odazvalo se 118 (68 %) davaoca. U postdonacijskom upitniku 8 davalaca je dalo podatak da su prethodno lečeni od sifilisa, dok većina davalaca nije isključila mogućnost rizičnog seksualnog kontakta. **Zaključak:** Kod 174 (0,041 %) testiranih davalaca utvrdjen je pozitivan potvrdni test. Analiza epidemioloških karakteristika seroreaktivnih davalaca može doprineti boljem razumevanju trendova infekcije i unapređenju preventivnih aktivnosti u transfuzijskoj medicini.

Ključne reči: dobrovoljni davaoci krvi, sifilis, imunoblot testiranje

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SYPHILIS IN VOLUNTARY BLOOD DONORS - RESULTS OF THE BLOOD TRANSFUSION INSTITUTE OF SERBIA

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Introduction: Syphilis represents a significant public health problem despite the availability of diagnostics and therapy. Transfusion services have an important role in preventing the transmission of infections by blood through mandatory screening of all blood units for Treponema pallidum. **Objective of the work:** Presentation and analysis of the frequency of confirmatory positive syphilis test results in the population of voluntary blood donors at the Blood Transfusion Institute of Serbia. **Material and methods:** A retrospective analysis of the results of syphilis testing performed on 420 098 blood donors in the period 2020-2025 was conducted. All tests were performed under the same conditions using automated platforms using ELISA and CMIA tests. In donors with repeat-reactive results of the screening test, according to the national testing algorithm, confirmatory testing with immunoblot tests was carried out. **Results:** A positive confirmatory test was obtained in 174 donors (0.041%), of which 154 (88.5%) were male and 20 (11.5%) were female. Confirmed positive results were detected in 94 (54 %) first-time donors , remaining 80 (46 %) in multiple donors. Confirmed positive results are most common in the age group of 31-40 years, with 54 donors (31.03%). Associated infection (HIV and HBV) was present in three donors. All confirmed positive donors were invited to the Counseling Center for blood donors, and 118 (68%) donors responded. In the post-donation questionnaire, 8 donors stated that they had previously been treated for syphilis, while the majority of donors did not exclude the possibility of risky sexual contact. **Conclusion:** A positive confirmatory test was found in 174 (0.041%) tested donors. Analysis of the epidemiological characteristics of seroreactive donors can contribute to a better understanding of infection trends and improvement of preventive activities in transfusion medicine.

Key words: voluntary blood donors, syphilis, immunoblot testing

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PRISUSTVO VIRUSA HEPATITISA E KOD DOBROVOLJNIH DAVALACA KRVI U SRBIJI: REZULTATI NAT-TMA SKRININGA I PROCENA RIZIKA TRANSFUZIJSKOG PRENOSA

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Uvod: Među dobrovoljnim davaocima krvi u Srbiji zabeležena je visoka seroprevalenca anti-HEV antitela (15%), međutim, do sada u analiziranim uzorcima nije detektovana HEV RNK. Virus hepatitisa E (HEV) predstavlja transfuzijski rizik u Evropi, zbog mogućnosti asimptomatske viremije. U Hrvatskoj je prevalenca HEV RNK približno 1:2158 donacija. Iako infekcija HEV-om kod imunokompetentnih osoba najčešće prolazi asimptomatski, prisustvo viremičnih dobrovoljnih davalaca krvi predstavlja potencijalni rizik za primaoce krvnih komponenti. Posebno su ugroženi imunokompromitovani pacijenti, primaoci transplantiranih organa, hematološki pacijenti, osobe na imunosupresivnoj terapiji i HIV pozitivni pacijenti. Pored toga, povećan rizik od teških kliničkih formi bolesti postoji kod osoba sa prethodno postojećim hroničnim oboljenjima jetre, kao i kod trudnica tokom trećeg trimestra trudnoće.
Materijal i metode: U studiju su uključeni uzorci plazme dobrovoljnih davalaca krvi prikupljeni u Institutu za transfuziologiju i hemobiologiju VMA, kao i terenskim prikupljanjem krvi od davalaca u Srbiji. Detekcija HEV RNK je rađena primenom ID NAT-TMA multiplex testova „Procleix UltrioPlex E assay" (Grifols, Procleix Panther system).
Rezultat: Rezultati će biti analizirani deskriptivnim statističkim metodama, a učestalost HEV viremije će biti izražena kao procenat pozitivnih uzoraka u odnosu na ukupan broj testiranih donacija.
Zaključak: Prisutnost HEV RNK kod dobrovoljnih davalaca krvi potvrdiće potrebu za kontinuiranim epidemiološkim praćenjem i razmatranjem uvođenja univerzalne NAT-TMA skrining strategije u cilju dodatnog unapređenja bezbednosti transfuzijskog lečenja u Srbiji.
Ključne reči: virus hepatitisa E (HEV), dobrovoljni davaoci krvi, NAT-TMA

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HEPATITIS E VIRUS DETECTION AMONG VOLUNTARY BLOOD DONORS IN SERBIA: RESULTS OF NAT-TMA SCREENING AND ASSESSMENT OF TRANSFUSION-TRANSMISSION RISK

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Background: Hepatitis E virus (HEV) is a transfusion-transmissible pathogen due to the possibility of asymptomatic viremia among blood donors. Although a high seroprevalence of anti-HEV antibodies (15%) has been reported among blood donors in Serbia, HEV RNA has not yet been detected in tested donations. In Croatia, the prevalence of HEV RNA-positive donations is approximately 1 in 2,158. While HEV infection is generally asymptomatic in immunocompetent individuals, transfusion-transmitted infection may pose a risk to immunocompromised patients, solid organ transplant recipients, hematology patients, individuals receiving immunosuppressive therapy, HIV-positive patients, pregnant women, and patients with chronic liver disease.
Materials and Methods: The study included plasma samples collected from voluntary blood donors at the Institute of Transfusiology and Hemobiology of the MMA and from donors recruited through mobile blood collection campaigns across Serbia. HEV RNA screening was performed using the ID NAT-TMA multiplex assay „Procleix UltrioPlex E assay" (Grifols, Procleix Panther system).
Results: Data will be analyzed using descriptive statistical methods. The prevalence of HEV viremia will be expressed as the proportion of HEV RNA-positive donations among all tested samples.
Conclusion: Detection of HEV RNA among blood donors would indicate ongoing circulation of HEV in the donor population and support consideration of routine NAT-TMA screening to improve transfusion safety and strengthen epidemiological surveillance in Serbia.
Keywords: Hepatitis E virus (HEV), blood donors, NAT-TMA.

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KAD SA VAMA PUTUJE SKRIVENI PUTNIK (PRIKAZ KLINIČKOG PRIMERA)

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Ključne reči (key words): malarija, davaoc, krv, pacijent ; malaria, donor, blood , patient

Malarija, iako endemična u tropskim i suptropskim područjima, u poslednjim godinama i u Sloveniji predstavlja značajan javnozdravstveni rizik, zbog putovanja ljudi. Bolest izaziva parazit (Plasmodium spp), a prenosi se na čoveka zaraženim komarcem Anopheles sp.. Simptomi bolesti uključuju temperaturu, drhtavicu, znojenje, glavobolju, mučninu i mogu brzo napredovati u teži oblik sa anemijom, otkazivanjem organa i smrt. Zbog mogućnosti prenosa malarije krvlju, izazov je i za transfuzijsku službu pri odabiru davaoca krvi, a u slučaju (teškog oblika) malarije izazov je i u lečenju pacijenta.
U Sloveniji, prema podacima Nacionalnog inštituta za javno zdravje, dosad se beleže samo uvezeni slučajevi malarije (u 2021 prijavljena su tri, u 2022 osam, u 2023 jedanaest, a u godini 2024 devet slučajeva), ali u poslednjem periodu primećuje se povećan broj prijema pacijenata sa malarijom, koje su se vratili iz tropskih i suptropskih područja, naročito iz Zanzibara. U 2025. godini oboljelo je devet, a u 2026 već četiri je prijavljenih pacienta sa malarijo (1 smrt).
Teška malarija, najčešće izazvana Plasmodium falciparum, je urgentno stanje sa visokim rizikom otkazivanja organa i smrti. Zbog česte slične kliničke slike, u odsustvu podataka o putovanju, može postojati ozbiljan rizik od odlaganja postavljanja dijagnoze i uvođenja ciljanog tretmana.
Prikazajemo primer teškog oblika Plasmodium falciparum malarije u Jedinici za intenzivnu negu Klinike za infektivne bolesti i febrilna stanja UKC Ljubljana. Pacijent je zbog višestrukog otkazivanja organa trebao intenzivnu suportivnu terapiju, uključujući i lečenje parenteralnim antimalarikom artesunatom. U lečenje je zbog visoke parazitemije dodatno uključena i izmenjajuća transfuzija, kao dodatna opcija spasilačkog lječenja.

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WHEN A HIDDEN PASSENGER TRAVELS WITH YOU (A CLINICAL CASE REPORT)

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Malaria, although endemic to tropical and subtropical areas, in recent years has also posed a significant public health risk in Slovenia, as a consequence of traveling. The disease, caused by a parasite (Plasmodium spp.), is transmitted to humans by an infected Anopheles sp.mosquito. Symptoms of the disease include fever, chills, sweating, headache, nausea, and can quickly progress to severe forms with anemia, organ failure, and death. Due to the possibility of malaria transmission through blood, it presents a particular challenge for transfusion service in selecting blood donors, and in cases of (severe) malaria, a challenge in supporting treatment for patient.
In Slovenia, according to National institute for Public health data, we record only imported cases of malaria ((in 2021, three cases were reported, in 2022 eight, in 2023 eleven, in 2024 nine cases), but recently we have observed an increased admission of patients with malaria, especially among individuals who have returned from tropical and subtropical regions, particularly from Zanzibar. In 2025, nine cases were treated, and in 2026, four malaria cases have already been recorded (1 fatal).
Severe malaria, most commonly caused by Plasmodium falciparum, is an urgent condition with a high risk of multi-organ failure and mortality. Due to the clinical presentation, in the absence of travel history, there may be a serious risk of delay in diagnosis and initiation of targeted treatment.
A case of severe Plasmodium falciparum malaria in the Intensive Care Unit of the Clinic for Infectious Diseases and Febrile Conditions at UKC Ljubljana will be presented. The patient required intensive supportive treatment due to multi-organ failure, including treatment with the parenteral antimalarial artesunate. In the treatment, due to high parasitemia, exchange transfusion was additionally included as an additional option for rescue therapy.
Key words: malaria, donor, blood , patient

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OPRAVDANOST PRIMENE RHD POZITIVNIH JEDINICA KRVI KOD RHD NEGATIVNIH PACIJENATA U FUNKCIJI PATIENT BLOOD MANAGEMENT-A I UPRAVLJANJA ZALIHAMA BOLNIČKE BANKE KRVI

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UVOD: Lečenje pacijenata zavisi od stabilnog snabdevanja komponentama krvi. Zalihe Rh(D)negativnih jedinica krvi posebno krvne grupe O najčešće su minimalne. Neophodno je unapređivati protokole za smanjenje upotrebe Rh(D) negativnih jedinica eritrocita implementacijom programa Patient Blood Managmenta (PBM).
CILJ RADA: Analiza upotrebe Rh(D)pozitivnih jedinica kod Rh(D) negativnih pacijenata u Bolničkoj banci krvi (BBK) KBC "Dr Dragiša Mišović-Dedinje" u cilju obezbeđivanja stabilnih zaliha krvi.
MATERIJAL I METODE: Retrospektivno su analizirani podaci iz informacionog sistema, protokola i dokumentacije BBK za period 01.01.2022.-31.12.2025. u odnosu na pol, starost, dijagnozu, odeljenje, broj primenjenih jedinica krvi i period primene.
REZULTATI: U četvorogodišnjem periodu ukupno je primenjeno 2358 jedinica komponenti eritrocita pacijentima koji su Rh(D) negativni, 1777 Rh(D) negativnih (75.3%) i 581 Rh(D) pozitivnih jedinica krvi (24.7%). Odluka o primeni Rh(D)+ krvi se donosi svakodnevno na osnovu raspoloživih rezervi BBK i potreba pacijenta. Rh(D)+ krv je primilo ukupno 260 pacijenata od koji je 52,7% muškog pola. Od ukupnog broja pacijenata 149 je sa odeljenja klinika za hirurgiju i urologiju, 105 sa odeljenja internih klinika i 6 sa ostalih. Na mesečnom nivou primenjuje se 15-62 Rh(D) negativnih i 1-35 Rh(D) pozitivnih jedinica, a ukupan broj RhD negativnih jedinica krvi koje se mesečno distribuiraju ka BBK kreće se od 11-55 jedinica.
ZAKLJUČAK: U skladu sa raspoloživim jedinicama krvi, starošću pacijenata i indikacijama primena Rh(D) pozitivne krvi Rh(D) negativnim pacijentima je opravdana kako bi se osigurala kontinuirana dostupnost Rh(D) negativnih jedinica za pacijentkinje u reproduktivnom period, imunizovane pacijente i za vitalne indikacije.
Ključne reči: Bolnička banka krvi, Transfuzija krvi

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THE RATIONALE FOR USING RHD-POSITIVE BLOOD UNITS IN RHD-NEGATIVE PATIENTS: A PATIENT BLOOD MANAGEMENT AND BLOOD INVENTORY MANAGEMENT

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INTRODUCTION: Patient treatment depends on a stable blood supply. Stocks of Rh(D) negative blood units, particularly group O are often limited. Patient Blood Management (PBM) programs may help reduce the use of Rh(D) negative red blood cell (RBC) units.
AIM: To analyze the use of Rh(D) positive RBC units in Rh(D) negative patients at the Hospital Blood Bank (BB) of the Clinical Hospital Center "Dr Dragiša Mišović-Dedinje" in order to ensure stable blood supplies.
MATERIAL AND METHODS: Data from the BB information system, protocols and documentation were retrospectively analyzed for the period January 1, 2022–December 31, 2025. Data were analyzed according to sex, age, diagnosis, hospital department, number of RBC units administered and period of administration.
RESULTS: During the four-year study period, 2358 RBC units were administered to Rh(D) negative patients: 1777 Rh(D) negative (75.3%) and 581 Rh(D) positive units (24.7%). The decision to administer Rh(D) positive blood was made daily according to available reserves and individual patient needs. A total of 260 patients received Rh(D) positive RBC units, of whom 52.7% were male. Of these, 149 patients were treated in surgical and urological departments, 105 in internal medicine departments, and 6 in other. On a monthly basis 15–62 Rh(D) negative and 1–35 Rh(D) positive RBC units were administered, while the total number of Rh(D) negative blood units distributed to the Blood Bank monthly ranged from 11 to 55.
CONCLUSION: Considering blood availability, patient age, and clinical indications, the use of Rh(D) positive RBC units in Rh(D) negative patients is justified to preserve Rh(D) negative units for women of reproductive age, alloimmunized patients, and life-threatening indications.
Key words: Blood Banks, Erythrocyte Transfusion

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UPOTREBA CELL SAVER-A TOKOM CARSKOG REZA ZBOG PATOLOŠKE PLACENTACIJE

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Uvod: Intraoperativno spasavanje krvi upotrebom cell savera (IOSK) tokom carskog reza (CS) kod pacijentkinja sa patološkom placentacijom (placenta praevia, accreta, increta,...) predstavlja zlatni standard u savremenom upravljanju masivnim krvarenjem ali se, zbog potencijalnog rizika od embolizma amnionskom tečnošću i opasnosti od aloimunizacije majke, njegova upotreba izbegava ili je minimalna. U našoj klinici IOSK je uveden marta 2022. i do aprila 2026. je urađeno 394 procedure, od kojih 137 tokom carskog reza zbog patološke placentacije.
Cilj rada: Prikaz iskustva primene cell savera tokom CS.
Metod: Uprkos uobičajenoj praksi korišćenja dve sukcione linije i prikupljanja krvi u rezervoar cell saver-a posle porađanja posteljice, zbog tehničkih ograničenja, krv je prikupljana od početka jednom sukcionom linijom, zajedno sa amnionskom tečnošću. Nakon procesiranja i pranja eritrocita, korišćen je filter za leukodepleciju pre reinfuzije eritrocita.
Rezultati: Prosečna starost porodilja je bila 35,2 godine (25-50), hemoglobin pre CS: 105,6 (80-138 g/l), sa parametrima hemostaze (PT, INR, aPTT i fibrinogen) u normalnom opsegu. Tokom procedure u rezervoar je prikupljeno između 350 i 3600ml (prosečno 1252 ml) i vraćeno pacijentkinjama 160-1830 ml (prosečno 553 ml) eritrocita. Posle transfuzije, hemoglobin meren nakon 24h, bio je između 65 i 135 g/l (prosečno 101 g/l). U deset slučajeva urađena je reintervencija, isti ili naredni dan, od kojih pet sa IOSK. Dato je 57 jedinica alogene krvi od čega 48 tokom reintervencije, a 9 porodiljama bez reintervencije. Neželjene reakcije nisu zabeležene.
Zaključak: Eritrociti prikupljeni i procesirani tokom IOSK, sa obaveznom primenom leukodeplecije pre reinfuzije, su sigurni i efikasni čak i kada se kolekcija krvi započne pre rađanja posteljice, zajedno sa amnionskom tečnošću.
Ključne reči: Placenta praevia, spasavanje krvi, cell saver

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USE OF CELL SAVER DURING CESAREAN SECTION WITH ABNORMAL PLACENTATION

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Introduction: Intraoperative cell salvage using a cell saver (IOCS) during caesarean section (CS) due to abnormal placentation is the gold standard in modern massive bleeding management, but since the potential risk of amniotic fluid embolism and maternal alloimmunization, its use is avoided or minimal. In our hospital IOCS is introduced on March 2022. and 394 procedures has been done until April 2026, 137 of which during CS because of abnormal placentation (Placenta praevia, accrete, increta…).
Goal: Presentation of the experience of using cell saver during CS.
Method: Despite a common practice to use two separate suction lines and collect blood into cell saver reservoir after delivery of placenta, due to technical reasons, blood is collected with one suction line, together with amniotic fluid. After processing and washing, leukodepletion filter was used before reinfusion.
Results: Average age of 137 treated parturients was 35,2 years (25-50), hemoglobin before CS: 105,6 g/l (80-138 g/l) with hemostasis parameters (PT, INR, aPTT and fibrinogen) within normal range. During IOCS in reservoir was collected between 350 and 3600 ml of blood (average 1252 ml) and reinfused 160 to 1830ml (average 553 ml) of erythrocytes. After transfusion, hemoglobin, measured after 24 hours, was between 65 and 135 g/l (average 101g/l). In ten cases reintervention was performed, same or consecutive day, five with IOCS. 57 unit of allogeneic blood was used, 48 of which during reintervention and 9 for four other parturient. No adverse events were detected.
Conclusion: Erythrocytes collected and processed within IOCS, with mandatory use of leukodepletion before reinfusion are safe and efficient even if collected before placenta delivery, together with some amniotic fluid.
Key words: placenta praevia, blood salvage, cell saver

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INTRAOPERATIVNO SPAŠAVANJE ERITROCITA I TROMBOCITA TOKOM HIRURŠKOG LEČENJA ANEURIZME ABDOMINALNE AORTE PRIMENOM ISEP TEHNOLOGIJE

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Uvod: Operacije aneurizme abdominalne aorte predstavljaju hirurške procedure sa visokim rizikom od značajnog perioperativnog gubitka krvi i potrebe za alogenim transfuzijama. Intraoperativno spašavanje krvi primenom ISEP (Intelligent System for Erythrocyte and Platelet Salvage) tehnologije omogućava prikupljanje, obradu i reinfuziju autolognih eritrocita i trombocita, čime se potencijalno smanjuje potreba za transfuzijom krvnih derivata.
Cilj: Procena efikasnosti ISEP tehnologije u očuvanju eritrocita i trombocita tokom operacija aneurizme abdominalne aorte, kao i njenog uticaja na potrebu za alogenim transfuzijama.
Materijal i metode: U studiju je uključeno 12 pacijenata podvrgnutih elektivnoj operaciji aneurizme abdominalne aorte. Tokom operacije korišćen je ISEP sistem za prikupljanje i obradu izgubljene krvi. Analizirani su perioperativni gubitak krvi, količina retransfundovanih eritrocita i trombocita, vrednosti hemoglobina i broja trombocita pre i nakon operacije, kao i potreba za alogenim transfuzijama alogenih eritrocita i trombocita.
Rezultati: Primena ISEP tehnologije omogućila je uspešnu reinfuziju značajne količine autolognih eritrocita ali i značajnu količinu trombocita, koje klasični Cell Saver aparati ne isporučuju. Kod većine pacijenata zabeleženo je očuvanje stabilnih postoperativnih vrednosti hemoglobina i trombocita, uz smanjenu potrebu za alogenim transfuzijama. Nisu registrovane ozbiljne komplikacije povezane sa primenom sistema.
Zaključak: ISEP tehnologija predstavlja bezbednu i efikasnu metodu intraoperativnog spašavanja eritrocita i trombocita tokom operacija aneurizme abdominalne aorte. Njena primena doprinosi smanjenju potrebe za alogenim transfuzijama i unapređenju perioperativnog zbrinjavanja pacijenata.
Ključne reči: aneurizma abdominalne aorte; autologna transfuzija krvi; čuvanje krvi; eritrociti; trombociti; transfuzija krvi; transfuzija krvnih komponenti; intraoperativno spasavanje krvnih ćelija; transfuzijska medicina; ISEP tehnologija.

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INTRAOPERATIVE ERYTHROCYTE AND PLATELET SALVAGE DURING ABDOMINAL AORTIC ANEURYSM REPAIR USING ISEP TECHNOLOGY

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Introduction: Abdominal aortic aneurysm surgery is a high-risk surgical procedure associated with significant perioperative blood loss and a substantial need for allogeneic blood transfusions. Intraoperative blood salvage using ISEP (Intelligent System for Erythrocyte and Platelet Salvage) technology enables the collection, processing, and reinfusion of autologous erythrocytes and platelets, thereby potentially reducing the need for allogeneic blood products.
Objective: To evaluate the efficacy of ISEP technology in preserving erythrocytes and platelets during abdominal aortic aneurysm surgery and to assess its impact on the requirement for allogeneic blood transfusions.
Materials and Methods: The study included 12 patients undergoing elective abdominal aortic aneurysm repair. During surgery, the ISEP system was used for the collection and processing of shed blood. Perioperative blood loss, the volume of retransfused erythrocytes and platelets, hemoglobin levels and platelet counts before and after surgery, as well as the need for allogeneic erythrocyte and platelet transfusions, were analyzed.
Results: The use of ISEP technology enabled the successful reinfusion of a significant quantity of autologous erythrocytes as well as a substantial number of platelets, which are not recovered by conventional Cell Saver systems. In most patients, stable postoperative hemoglobin levels and platelet counts were maintained, accompanied by a reduced need for allogeneic transfusions. No serious complications related to the use of the system were observed.
Conclusion: ISEP technology represents a safe and effective method for the intraoperative salvage of erythrocytes and platelets during abdominal aortic aneurysm surgery. Its use contributes to reducing the need for allogeneic transfusions and improving perioperative patient management.
Keywords: Abdominal Aortic Aneurysm; Blood Cell Salvage; Autologous Blood Transfusion; Erythrocytes; Platelets; Blood Conservation; Blood Transfusion; Transfusion Medicine; ISEP Technology.

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IMUNOHEMATOLOŠKI UZROCI TEŠKE ANEMIJE FETUSA

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Uvod: Intrauterina intravaskularna transfuzija krvi (IUT) je terapijska prenatalna procedura koja se primenjuje u lečenju teške fetalne anemije, najčešće nastale zbog hemolizne bolesti fetusa (HBF) usled aloimunizacije majke eritrocitnim antigenima fetusa. HBF može dovesti do teške anemije fetusa, fetalnog hidropsa i intrauterine smrti, ako ne bude prepoznata na vreme i ne primeni se IUT.
Cilj rada: Cilj rada je analiza uzročnika koji su doveli do anemije fetusa koja je zahtevala IUT kao terapiju.
Materijal i metod: Analizirani su podaci trudnoća komplikovanih fetalnom anemijom koje su zahtevale IUT kao terapijsku meru. Podaci su prikupljeni iz protokola IUT kao i medicinskih kartona trudnica koje su lečene na Klinici za ginekologiju i akušerstvo, Univerzitetskog kliničkog centra Srbije, u periodu od 2002. god. do 2026. god.
Analizirani su sledeći parametri: specifičnost antieritrocitnih antitela, fetalni hematokrit (Hct) pre i posle IUT, gestacijska starost pri prvoj i poslednjoj IUT i broj IUT procedura tokom trudnoće.
Specifičnost antitela se utvrđuje metodom u gelu (ID-Card Coombs anti-IgG, BioRad, DiaMed GmbH, Switzerland) sa odgovarajućim panelima eritrocita (ID-DiaPanel/ID-DiaPanel-P, BioRad, DiaMed GmbH, Switzerland).
Fetalni Hct se utvrđije metodom mikrohematokrita po Clay-Adams-u, upotrebom heparinizranih cevčica promera 70 x 1mm i mikrohematokrit centrifuge (12.000 obrtaja, 1minut).
Rezultati: Kod 41 trudnice urađeno je ukupno 152 IUT. Anti RhD-antitelo je identifikovano u 95% slučajeva. Prva IUT je u proseku rađena u 26 g.n., poslednja u 33 g.n. Prosečan porast Hct je bio 18%.
Zaključak: Najzastupljenije antitelo je bilo anti-RhD antitelo. Kod trudnoća u kojima je HBF nastala kao rezultat prisustva više antieritrocitnih antitela, anemija fetusa je bila teškog stepena, prva IUT je izvođena ranije u toku trudnoće i bio je potreban veći broj IUT u poređenju sa HBF prouzrokovanih prisustvom jednog antitela.
Ključne reči: Intrauterina transfuzija krvi, Hemolizna bolest fetusa i novorođenčeta, Aloimunizacija

UP 51

IMMUNOHEMATOLOGICAL CAUSES OF SEVERE FETAL ANEMIA

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Introduction: Intrauterine intravascular blood transfusion (IUT) is a therapeutic prenatal procedure used to treat severe fetal anemia, most commonly caused by hemolytic disease of the fetus (HDF) due to maternal alloimmunization to fetal red blood cell antigens. HBF can lead to severe fetal anemia, fetal hydrops, and intrauterine death if not recognized and treated with IUT in time.
Aim: Analysis of the causes that led to fetal anemia that required IUT as therapy.
Material and method: The data for pregnancies complicated by fetal anemia that required IUT as a therapeutic measure were analyzed. Data were collected from IUT protocols as well as medical records of pregnant women who were treated at the Clinic for Gynecology and Obstetrics, University Clinical Center of Serbia, in the period from 2002. until 2026.
The following parameters were analyzed: specificity of antierythrocyte antibodies, fetal hematocrit (Hct) before and after IUT, gestational age at the first and last IUT and number of IUT procedures during pregnancy.
Antibody specificity is determined by gel method (ID-Card Coombs anti-IgG, BioRad, DiaMed GmbH, Switzerland) with appropriate erythrocyte panels (ID-DiaPanel/ID-DiaPanel-P, BioRad, DiaMed GmbH, Switzerland).
Fetal Hct is determined by the microhematocrit method according to Clay-Adams, using heparinized tubes with a diameter of 70 x 1mm and a microhematocrit centrifuge (12,000 revolutions for 1 minute).
Results: A total of 152 IUTs were performed in 41 pregnancies. Anti RhD-antibody was identified in 95% of cases. On average, the first IUT was performed at 26 gestational weeks, the last at 33 gestational weeks. The average increase in Hct was 18%.
Conclusion: The most frequent antibody was anti-RhD antibody. In pregnancies in which HBF resulted from the presence of multiple antierythrocyte antibodies, the fetal anemia was severe, the first IUT was performed earlier in pregnancy, and a greater number of IUTs were required compared to HBF caused by a single antibody.
Key words: Intrauterine transfusion, Hemolytic disease of the fetus and newborn, Alloimmunization

UP 52

PATIENT BLOOD MANAGEMENT NA REGIONALNOM NIVOU – MIT ILI STVARNOST

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Uvod: Patient Blood Management (PBM) je je sistematski pristup usmeren prema pacijentu, zasnovan na dokazima koji čuva i koristi pacijentovu sopstvenu krv a isto vreme unapređuje pacijentovu bezbednost i oporavak .
Materijal i metode: U retrospektivnoj observacionoj studiji, iz protokola operativnog programa, protokola spasene krvi i protokola izdate krvi transfuzije uporedili smo podatke u obasti ortopedije, urologije i vaskularne hirurgije za 2014/2019 sa podacima iz 2024 i 2025.godine. Podaci se odnose na period kada se program PBM sprovodio u delovima ili nikako sa podacima gde se u ovim oblastima sprovodi kao standardna mera. Od metoda deskriptivne statistike koristili smo srednju vrednost, medijanu, standardnu devijaciju, maksimalnu i minimalnu vrednsost.
Cilj rada je da ispita da li principi Patiemt Blood Managementa -PBM doprinose tj smanjuju neracionalnu upotrebu krvi i komponanata a u cilju boljeg oporavka pacijenata.
Rezultati: U pilot studiji iz 2014 za 27 ortopedskih pacijenata utrošeno je 11 jedinica eritrocita i 4 jedinice plazme (ZSP). U 2025 za 270 ortopedskih pacijenata izdato je 12 jedinica eritrocita bez plazme. U oblasti vaskularne hirurgije broj izdatih jedinica krvi za period od 2014 do 2022 je 18 jedinica eritrocita i 27 jedinica ZSP, za 20 pacijenata. U periodu od 2022 do 2024 izdato je 7 jedinica eritrocita, 7 ZSP za 29 pacijenata. Kod uroloških pacijenata sa suprapubičnim operacijama prostate u 2019.godini, za 18 pacijenata izdato je 8 jedinica eritrocita i 8 jedinica plazme, u 2025 za 30 pacijenata 4 jedinice eritrocita, bez plazme perioperativno. Prema vodiču Svetske Zdravstvene Organizacije za sprovodjenje PBM,zadužen je klinički lekar koji uspeva da prebrodi otpor koji može da se javi na organizacionom nivou.
Zaključak : Analiza naših rezultata pokazala je da PBM pristup značajno smanjuje primenu alogene krvi, da se kompletno uspostavljanje ovih mera može sprovesti uz podršku Ministarstva Zdravlja , kao i udruženja hirurije i anestezija. Najbezbednija krv je ona koja nije data pacijentu.
Ključne reči : Patient blood Management, smanjenje neracionalne upotrebe alogene krvi,

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PATIENT BLOOD MANAGEMENT ON REGIONAL LEVEL – MYTH OR REALITY

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Introduction: Patient blood management (PBM) is a patient-centered, systematic, evidence-based approach to improve patient outcomes by managing and preserving a patient's own blood, while promoting patient safety and empowerment.
Material and methods: In retrospective, observational study, from records of operating theater, records of cell savings and records of crossmatches from blood bank, we compare data from departments of orthopedics, urology and vascular surgery for 2014/2019 and 2024/2025. Data were related to period when PBM was introduced partially or none to data when PBM was implemented as standard. We use descriptive statistics such as mean, median, SD, maximal and minimal values.
The Aim of this study is to assess how methods of Patient Blood Management reduce unnecessary transfusions of RBC without harm for patients.
Results: According to pilot study from 2014, 27 orthopedic patients were demanded with 11 units of Red Blood cells (RBC) and 4 units of fresh frozen plasma (FFP). In 2025, for 270 patients, 12 units of RBC were used and no FFP. In vascular surgery, number of RBC issued for 20 patients, in period from 2014 to 2022 was 18 units and 27 units of FFP. For 29 patients, from 2022 to 2024, number of RBC was 7 and FFP was 7. In 2019, 18 suprapubic prostate surgery patients spent 8 units RBC and 8 units FFP. In 2025, for 30 patients were issued 4 units of RBC, no FFP perioperatively. According to guidelines of WHO, for implementation of principles of PBM, clinical doctors in this area should be dedicated to spreading initiative and people who can absorb resistance on organizational level.
Conclusion: Analysis of these results has shown that PBM approach can significantly reduce usage of allogeneic blood, and that implementation on national level can be achieved with help of Ministry of Health and societies of Anesthesia and Surgery. The Safest blood is one that is not given to patients.
Key words: Patient blood Management, reduce of unneccesarry blood transfusion

UP 53

TRANSFUZIJSKA PRAKSA KOD NEONATUSA I PEDIJATRIJSKIH PACIJENATA U ZAVODU ZA TRANSFUZIJSKU MEDICINU FBIH

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UVOD: Transfuzija krvnih produkata neonatusima i pedijatrijskim pacijentima ima mnogo zajedničkog sa transfuzijom odraslim pacijentima, ali postoje i određene razlike. Značajni faktori su: a) mali ukupni volumen krvi, b) nezreo koagulacijski i imunološki sistem, c) jedinstvena stanja koja zahtjevaju transfuzijsko liječenje.
CILJ/SVRHA: Cilj ove retrospektivne studije je prikazati iskustva i transfuzijsku praksu kod neonatusa i pedijatrijskih pacijenata u našoj ustanovi tokom desetogodišnjeg perioda.
MATERIJAL I METODA: Retrospektivna analiza provedena je korištenjem podataka iz Informacionog sistema Zavoda za period od 10 godina (2016-2026). Analizirani su: broj pacijenata, broj izdatih krvnih komponenti, te zastupljenost pojedinih vrsta krvnih komponenti. Dobijeni podaci obrađeni su deskriptivnim statističkim metodama.
REZULTAT: Imunohematološke analize urađene su za 12.796 pacijenata, od čega je 4.374 (32%) neonatusa. Krvni produkti izdati su za 8.974 pacijenata.
Ukupno je izdato 15.590 krvnih komponenti, uključujući 5.553 (35,6%) eritrocitna pripravka, 5.492 (35,2%) jedinice svježe smrznute plazme i 4.545 (29,2%) koncentrata trombocita. Od eritrocitnih pripravaka izdato je 5.220 koncentrata eritrocita, 263 jedinice ozračenih koncentrata eritrocita i 70 jedinica pune krvi. Filtrirani eritrocitni pripravci činili su 5.413 (97%) svih eritrocitnih pripravaka. Od ukupno 4.545 trombocitnih koncentrata, 1.254 (27,6%) bila su ozračena, a 558 (12,3%) filtrirana.
ZAKLJUČAK: Dobijeni rezultati ukazuju na dosljednu primjenu preporuka za transfuzijsko liječenje neonatusa i pedijatrijskih pacijenata usmjerenih ka povećanju sigurnosti i unapređenju kvaliteta transfuzijskog liječenje ove osjetljive populacije.
KLJUČNE RIJEČI: Transfuzija krvnih komponenti; Novorođenčad, djeca; Pedijatrija

UP 53

TRANSFUSION PRACTICE IN NEONATES AND PEDIATRIC PATIENTS IN BLOOD TRANSFUSION INSTITUTE OF THE FBIH

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BACKGROUND: Transfusion of blood components in neonates and pediatric patients has many commonalities with that of adult patients; however, there are significant differences. Elements to consider are a) small total blood volume, b) immature coagulation and immune system, c) unique conditions requiring transfusion therapy.
AIM AND OBJECTIVE: The aim of this study is to present experiences and transfusion practices regarding neonates and pediatric patients in our institution during a ten-year period.
MATERIALS AND METHODS: This study is conducted based on data obtained from the IT System of our facility during the ten-year period (2016-2026). Number of patients, number of used blood components and distribution of individual blood components. The obtained data were analyzed using descriptive statistical methods.
RESULTS: Immunohematology analyses were performed for 12.796 patients, of which 4.374 (32%) were neonates. Blood components were issued for 8.974 patients.
A total of 15.590 blood components were issued, including 5.553 (35,6%) red blood cell components, 5.492 (35,2%) FFP units, and 4.545 (29,2%) platelet concentrates.
From the total number of red blood cell components, 5.220 packed red blood cells, 263 irradiated packed red blood cells and 70 whole blood units were issued. Leukoreduced red blood cell components accounted for 5.413 (97%) of all red blood cell components.
From the total of 4.545 platelet concentrates, 1.254 (27,6%) were irradiated, and 558 (12,3%) leukoreduced.
CONCLUSION: Results indicate the consistent adherence to transfusion recommendations regarding neonates and pediatric patients aimed at increasing security and improving quality of transfusion therapy in this sensitive population.
KEYWORDS: Blood Component Transfusion; Infant, Newborn; Child; Pediatrics

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ZNAČAJ PRIMENE REHIDRATACIONE TERAPIJE PRE TRANSFUZIJE KRVI PREKO VENSKOG PORTA KOD ONKOLOŠKIH PACIJENATA

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UVOD. Transfuzija krvi kod onkološki pacijenata se primenjuje u svrhu nastavka specifičnog onkološkog lečenja. **Venski port** je mali medicinski uređaj koji se ugrađuje pod kožu i omogućava bezbedan, dugotrajan i bezbolan pristup venskom sistemu onkoloških pacijenata. Namenjen je za primenu hemioterapije, transfuzija, uzorkovanje krvi i primenu ostale terapije.
CILJ. Osnovni cilj istraživanja je analiza bezbedne primene krvi preko venskog porta.
MATERIJAL I METODE. Istraživanje je sprovedeno kao deskriptivno-retrospektivna studija. U ispitivanje su uključeni pacijenti kojima je zbog insuficijencije venskih puteva , kao posledica primene hemioterapije , implementiran venski port. Pacijenti su ambulantno na našem odeljenju dolazili za primenu krvi u periodu od decembra 2025. do maja 2026. godine kako bi nastavili sa specifičnim onkološkim lečenjem.
REZULTAT. Kod pacijenata koji nisu dobili rehidratacionu terapiju pre transfuzije, transfuzija krvi je trajala oko 3 sata po primenjenoj jedinici. A kod pacijenata kod kojih je primenjeno 100 ml fiziološkog rastvora, transfuzija je ubrzana za 15 minuta po jedinici krvi, dok kod pacijenata kod kojih je primenjeno 250 ml fiziološkog rastvora transfuzija jedne jedinice je trajala 2 sata.
ZAKLJUČAK. Bezbedna primena krvi po jedinici je od 1 i po do 2 sata, ne duže od 4 sata. Primenom fiziološkog rastvora značajno je ubrzano vreme trajanja transfuzije i obezbeđena je bezbednost primene krvi.
KLJUČNE REČI. transfuzija, venski port, rehidrataciona terapija

UP 54

THE IMPORTANCE OF THE APPLICATION OF REHYDRATION THERAPY BEFORE THE TRANSFUSION OF BLOOD THROUGH THE PORT OF VENUS IN ONCOLOGICAL PATIENTS

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INTRODUCTION. Transfusion of blood in oncological patients is used for the purpose of continuing specific oncological treatment. A venous port is a small medical device that is implanted under the skin and provides safe, long-term and painless access to the venous system of oncology patients. It is inteded for the application of chemotherapy, transfusion, blood sampling and the other therapies.
OBJECTIVE. The main objective of the research is the analysis of the safe administration of blood through the venous port.
MATERIAL AND METHODS. The research was conducted as a descriptive-retrospective study. The study included patients who, due to venous insufficiency, as a result of chemotherapy, had a venous port implemented. Patients came to our department on an outpatient basis for blood transfusion from december 2025. to may of 2026. in order to continue with specific oncological treatment.
RESULT. In patients who did not recive rehydratation therapy before transfusion, blood transfusion lasted about 3 hours per administered unit. And in patients who recived 100 ml of saline, tre transfusion was accelerated by 15 minutes per unit of blood, while in patients who recive 250 ml o fsaline, the transfusion of one unit lasted 2 hours.
CONCLUSION. Safe application of blood per unit is from 1 and a half to 2 hours , no longer than 4 hours. The use of physiological solution significantly accelerated the duration of transfusion and ensured the safety of blood administration.
KEY WORDS. Transfusion, venous port, rehydration therapy

8. KONGRES
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APSTRAKTI / ABSTRACTS

POSTER PREZENTACIJE / POSTER PRESENTATIONS

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Beograd, SRBIJA / Belgrade, Serbia
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PP 001

NEŽELJENE REAKCIJE KOD DAVALACA KRVI U ZAVODU ZA TRANSFUZIJSKU MEDICINU REPUBLIKE SRPSKE

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UVOD: Iako je dobrovoljno davanje krvi bezbjedna i sigurna procedura koja je ograničena na zdrave osobe, ipak u malom broju slučajeva neizbježna je pojava neželjenih reakcija.
CILJ: Utvrditi težinu neželjenih reakcija kod dobrovoljnih davalaca krvi i definisati tip nastanka sa osvrtom na pol , uzrast, vrijeme javljanja i učestalost doniranja .
MATERIJAL I METODE: Retrospektivnom studijom je analiziran period od 01.01.2023.god do 31.12.2025.god u ZZTM RS Banja Luka u kojoj je učestvovalo 42.700 dobrovoljnih davalaca krvi .
REZULTATI: U navedenom periodu je prijavljeno 420 neželjenih reakcija kod 42.700 davalaca krvi tako da je incidenca 0,98%, odnosno,javi se 9,8 neželjenih reakcija na 1000 davalaca. Najveći broj reakcija imali su davaoci prosječne starosti 26 ± 8,6 godina, dominantno muškog pola 298 (70,95%), dok je žena bilo 122 (29,05%). Neželjene reakcije su se najčešće javljale u toku davanja krvi i to kod osoba koje prvi put daruju krv jer su oni u većem riziku da dožive neželjenu reakciju i njih je bilo 259 (61,66%), a višestrukih davalaca 161(38,4%). Prema lokalizaciji, dominantne su bile sistemske reakcije (vazovagalne reakcije, sinkopa, mučnina, hiperventilacija) kod 396 (94,28%) davalaca , dok su se lokalne reakcije (hematom,punkcija arterije,tromboflebitis,povreda nerava) javile kod 24(5,72%). U odnosu na težinu reakcije blagih reakcija (hematom,slabost i nesvjestica) je bilo 376(89,5%), a umjerenih (mučnina,preznojavanje) 44 (10,47%), dok težih reakcija u vidu kolapsa sa konvulzijama ili zastoja srca nije bilo.
ZAKLJUČAK: Rezultati studije su pokazali da u našoj ustanovi postoji niska učestalost neželjenih reakcija kod dobrovoljnih davalaca krvi.
KLJUČNE RIJEČI: neželjene reakcije, dobrovoljni davalac, hemovigilanca

PP 001

ADVERSE REACTIONS AT BLOOD DONORS IN THE INSTITUTE FOR TRANSFUSION MEDICINE OF THE REPUBLIKA SRPSKA

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INTRODUCTION: Although voluntary blood donation is a safe and secure procedure limited to healthy individuals, a small number of adverse reactions are still inevitable and can occur before, during, or after the donation.
OBJECTIVE: To determine the severity of adverse reactions in blood donors, to define the type of occurrence referring to gender, age, time of occurrence and frequency of donations.
MATERIAL AND METHODS: A retrospective study analysed the period from 1.01.2023. to 31.12.2025. in The Institute for Transfusion Medicine of the Republika Srpska in Banja Luka, in which 42.700 of voluntary blood donors participated.
RESULTS: During the mentioned period, 420 adverse reactions were reported in 42.700 blood donors, so the incidence of adverse reactions is 0,98% or 9,8 per 1000 donors. The majority of reactions occurred in donors with an average age of 26 ± 8.6 years, predominantly male 298 (70.95%), while the number of women was 122 (29.05%). Adverse reactions most frequently occurred during blood donation, especially in first-time donors, as they are at higher risk of experiencing an adverse reaction, and there were 259 (61,66%) first-time donors, and 161 (38,4%) multiple donors. According to localization, systemic reactions (vasovagal reactions, syncope, nausea, hyperventilation) were dominant in 396 donors (94.28%), while local reactions (hematoma, arterial puncture, thrombophlebitis, nerve injury) occurred in 24 donors (5.72%). In terms of reaction severity, mild reactions (hematoma, weakness and fainting) occurred in 376 (89.5%), and moderate reactions (nausea, sweating) in 44 (10.47%), while there were no severe reactions in the form of collapse with convulsions or cardiac arrest.
CONCLUSION: Study results showed that in our institution there is a low frequency of adverse reactions in voluntary blood donors.
KEY WORDS: adverse reactions, voluntary donor, hemovigilance

PP 002

TRENDS IN VOLUNTARY BLOOD DONATION AT THE DEPARTMENT OF TRANSFUSION MEDICINE STRUMICA, REGIONAL CENTER FOR TRANSFUSION MEDICINE SHTIP, INTITUTE FOR TRANSFUSION MEDICINE SKOPJE, MACEDONIA (2022-2025)

Prim.spec.dr. Deniza Stambolieva Departmenent of Transfusion medicine Strumica
Prim. Dr. spec. Meri Shorova, Dr. spec. Natali Jovanova,
Dr. spec. Boris Panev Regional Center for transfusion medicine Shtip

Introduction: Voluntary blood donation represents the foundation of safe and stable blood supply system. Monitoring donation trends supports transfusion services planning and donor and donor recruitment strategy.
Aim: To analyze trends and characteristics of blood donors in the Department of Transfusion Medicine Strumica, during 2022-2025.
Material and methods: A retrospective descriptive analysis was preformed using annual reports from the Department of Transfusion Medicine Strumica. Data included collected blood units, donor type, gender distribution, first time donors, mobile blood donation campaigns, and demographic characteristics.
Results: During four years, 6195 blood units, were collected. The highest number was recorded in 2024(1598), lowest in 2025 (1499). Voluntary donors accounted for over 95% annually. Male donors predominated - 77-80%, while female participation increased, reaching 22,7 % in 2025. Mobile campaigns supported blood collection, especially in 2023 and 2024. First time donors ranged from11,9% to 15,6%, demonstrating continuous recruitment of new donors. Employed individuals formed the largest donor group. Adverse reactions were rare; the lowest deferral rate was recorded in 2024 (2,7%)
Conclusion: Findings demonstrate a stable blood donation system in Strumica. Mobile campaigns remain important, while further educational activities may increase participation among women and young donors

PP 002

PP 003

THE PREVALENCE OF C ANTIGEN IN RHD NEGATIVE BLOOD DONORS IN STRUGA MUNICIPALITY, REPUBLIC OF NORTH MACEDONIA

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INTRODUCTION: The Rh blood group system, containing 56 antigens, is highly polymorphic and second in clinical importance after ABO blood group system. Among Rh antigens, D, c, E, C and e; differ in immunogenicity and may induce alloimmunization following transfusion or pregnancy. Knowledge of antigen distribution in local populations is essential for improving transfusion safety. In our setting, extended Rh typing is not fully implemented; however, D-negative donors are routinely tested for the C antigen.
AIM: To determine the prevalence of RhD and RhC antigens among voluntary blood donors in Struga Municipality.
MATERIALS AND METHODS: A retrospective analysis of data of 13,744 voluntary blood donations collected between 2019 and 2025 from two transfusion services in Struga, North Macedonia. Blood samples were analyzed using column agglutination gel cards (ID-Microtyping System) and slide testing with monoclonal anti-C antisera. The data was obtained from the national e-Delphyn system.
RESULTS: Of 13,744 donations, 1,710 (12%) were RhD-negative, corresponding to 497 donors. Among these, 56 donations (3.3%), from 22 donors, were C antigen positive. ABO distribution among RhD-negative donations was: O 631 (36.9%), A 622 (36.4%), B 296 (17.3%), and AB 161 (9.4%). The prevalence of the C antigen within these groups was 3.1% (O), 4.6% (A), 0.3% (B) and 3.7% (AB).
CONCLUSION: RhD-negative frequency is slightly lower than national average. The low prevalence of C antigen aligns with expected distributions, with notably rare occurrence in B and AB groups. Implementation of expanded Rh typing is needed to better define phenotypic distribution and improve transfusion compatibility.
Key words:Rh blood group system; RhD-negative donors; C antigen; antigen prevalence; blood donor population; transfusion safety

PP 003

PP 004

WHAT TRANSFORMS A FIRST -TIME DONOR INTO A REGULAR BLOOD DONOR

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Introduction: Maintaining a stable and safe blood supply remains a continuous challenge for transfusion services. In addition to recruiting new donors, it is equally important to retain them and encourage their transformation into regular voluntary blood donors. Understanding the factors that influence donor motivation, satisfaction and repeated donation plays a key role in ensuring a sustainable blood supply and improving transfusion practise.
Aim: To analyze the factors influencing repeated blood donation and the transformation of first-time donors into regular donors.
Material and methods: A retrospective analysis of data from Transfusion Medicine service Strumica was performed for the period 2022-2025.Additionally, an anonymous survey was conducted among 120 voluntary blood donors, including 60 first- time and 60 regular donors, to identify factors influencing repeated donation.
Results: A total of 6185 blood donations were registered during the analyzed period..The number of first- time donors gradually declined from 237 in 2022 and 2023, to 197 in 2024 and 179 in 2025.First time donors were more influenced by humanitarian motives, organized campaigns, a social influence, while regular donors emphasized positive donation experience, trust in staff and personal responsibility. The most important factors influencing repeated donations were positive first donation experience (78%), staff attitude (74%), the feeling of helping and saving lives (71%)and good organization of donation campaigns 9 62%). Two days off work after donation were a motivating factor for 41 %of respondents. Longer waiting time negatively influenced repeated donation in 32%. Motivation brings the donor once, but positive experience brings the donor back.
Conclusion: Regular blood donors are created through trust, positive experience and continuous communication. Understanding these factors may help improve donor retention strategies and maintain a stable donor base. Reducing waiting times through an increased number of trained phlebotomists and laboratory staff may improve donor satisfactions and encourage repeated blood donation.

PP 004

PP 005

NINETEEN YEARS OF ADVERSE TRANSFUSION REACTIONS IN THE REPUBLIC OF NORTH MACEDONIA

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Background: Haemovigilance covers the entire transfusion chain, from blood collection to recipient follow-up and is essential for identifying and preventing transfusion-related adverse events to improve transfusion safety.
Aim: To analyze adverse transfusion reactions (ATRs) reported to the Quality Assurance and Quality Control (QAQC) Department of the Institute for Transfusion Medicine of the Republic of North Macedonia (ITM).
Methods: A retrospective review of monthly and annual haemovigilance records was performed for all ATRs reported to the QAQC Department between 2007 and 2025.
Results: During the 19-year study period, 36 ATRs were reported. The most common reactions were mild allergic and febrile non-haemolytic transfusion reactions, presenting with urticarial rash, fever, dyspnea, tachycardia and nausea. No transfusion-related deaths were recorded. Reported adverse reactions by year were: 2007 – 2 (Cryoprecipitate and FreshFrozenPlasma(FFP)); 2008 – 1 (FFP); 2009 – 1; 2010 – 1 (FFP); 2011 – 3 (2 RedCell-Concentrate(RCC) and 1 FVIII concentrate); 2012 – 1 (Cryoprecipitate); 2013 – 2 (RCC and Cryoprecipitate); 2014 – 1 (Cryoprecipitate); 2015 – 1 (FFP); 2018 – 4 (1 FFP and 3 RCC); 2019 – 3 (FFP); 2020 – 4 (1 platelet concentrate and 3 RCC); 2021 – 1 (RCC); 2022 – 4 (RCC); 2023 – 2 (RCC); 2024 – 1 (RCC); and 2025 – 4 (2 RCC and 2 FFP).
Conclusions: Adverse transfusion reactions remain underreported, limiting opportunities to improve patient safety and transfusion practice. Strengthening haemovigilance through education, standardized reporting and robust surveillance systems is essential for timely recognition of adverse events, evidence-based decision-making and safer transfusion therapy.
Keywords: haemovigilance; adverse transfusion reactions; blood transfusion.

PP 005

PP 006

PREVALENCE OF IRREGULAR RBC ANTIBODY IN MACEDONIAN BLOOD DONORS

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Screening for irregular RBC antibody is mandatory test for every blood donation in accordance with national blood testing strategy. The aim of this study was to determine the prevalence, specificity and frequency of irregular red blood cell (RBC) antibodies detected using column agglutination technology (CAT) based on indirect antigobulin test (IAT) in routine blood donor screening.
A total of 252 641 blood donations collected between 2020 and 2024 were screened using pooled screening cells and gel-based automated system immune-hematological analyzer (IH 500/1000). Antibody specificity was determined in positive samples using commercially available 11-cell identification panel. Donations were obtained from 205 532 male donors (81%), 47 109 female donors (19%) and 47 919 were from first time donors (17%).
Irregular RBC antibodies were confirmed in 119 donations (119/252 641) corresponding to an overall prevalence of 0,05%. Of these, 88 % had defined specificity, while 12% were unspecified. The most frequently detected antibody was anti-M (33%), followed by antibodies of the Rh system (22%) and anti-K (15%) antibodies. Antibodies of the Rh system were anti-D (8%), anti-C (2%), anti-E (9%) and anti-c (3%). Less frequent antibodies were anti-P1 and anti-C^w (4% each), anti-Le^a (3%), then anti-Le^b, anti-Lu^a and anti-S (2% each) and the lowest frequency had anti-Fy^a and anti-Jk^a (1% each).
Female donors showed a significantly higher prevalence of irregular RBC antibodies (0,11%) than male donors (0,03%). The most frequent anti-M antibody has similar representation in both gender, 0.015% in males and 0,016% in female donors, as a result of the rejuvenation of our donor pool. Also in female donors more frequent antibodies were anti-K with 0,03%, anti-D with 0,02% and anti-E with 0,01%. Occurrence of two identified specific irregular RBC (anti-D+C) antibodies were detected in female donors. According to the results donors with positive direct antiglobulin test (DAT) were more frequent also in female donors (0,02%) in comparison with male donors (0,01%).
The low prevalence observed reflects effective donor selection and sensitive screening methods. Identification of clinically significant antibodies remains essential for ensuring transfusion safety and preventing hemolytic transfusion reactions.
Keywords: Antibody screening, irregular RBC antibodies, column agglutination technology (CAT), indirect antiglobulin test (IAT), delayed hemolytic transfusion reactions (DHTR)

PP 006

PP 007

ANALYSIS OF BLOOD DONATION PATTERNS AND DONOR PROFILE IN BTS –GOSTIVAR-A THREE –YEAR RETROSPECTIVE STUDY (2023-2025)

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Background: Blood donation is an essential component of transfusion medicine and plays a crucial role in ensuring a safe and adequate blood supply. Regular analysis of donor characteristics and donation patterns provides important information for improving donor recruitment and maintaining blood availability. **Aim:** The aim of this study was to analyze and compare blood donation activities during 2023, 2024 and 2025 in the Blood Transfusion Service in Gostivar (BTS-Gostivar). **Materials and Methods:** Data was obtained from the E-Delfin information system used in BTS-Gostivar. Annual records of blood donations from January 1, 2023 to December 31, 2025 were retrospectively analyzed. Donors were evaluated according to gender, donor status (first-time and repeat donors), type of donation, employment status, nationality and temporary donor deferral. **Results:** A total of 1,326 donations were recorded in 2023, 1,277 in 2024, and 1,409 in 2025, showing a decline in 2024 followed by an increase in 2025. Voluntary donation remained predominant (>99% in all years), while family donations were minimal (≤0.9%). Male donors consistently predominated, accounting for 90.2%, 89.5% and 90.3% in 2023, 2024 and 2025, respectively. First-time donors represented 12.0% (159), 14.1% (180) and 12.5% (176), while repeat donors remained the main source of blood supply (>85% in all years). Temporarily deferred donors were 18 in 2023, 39 in 2024 and 16 in 2025, mainly due to low hemoglobin, abnormal blood pressure, antibiotic therapy, surgery, allergies, and tattoos. Employed individuals represented the majority of donors (83.1%, 86.6%, and 81.6%). Regarding ethnic distribution, Albanian donors represented the largest group in 2025 (50.6%), followed by Macedonian donors (39.4%), while similar trends were observed in previous years. **Conclusions:** Blood donation activity in BTS-Gostivar remained relatively stable during the three-year period, with a temporary decline in 2024 followed by recovery in 2025. Voluntary and repeat donors continue to represent the backbone of the blood supply system. A gradual increase in the proportion of Albanian donors and fluctuations in first-time donor rates highlight the importance of continuous targeted recruitment and donor education. Variability in donor deferrals emphasizes the need for strict donor selection criteria to ensure a safe and sufficient blood supply.

Keywords: blood donation, voluntary blood donors, first-time donors, repeat donors, donor deferral, transfusion medicine, Gostivar.

PP 007

PP 008

KLINIČKA REVIZIJA-KONTROLA MJERENJA VRIJEDNOSTI HEMOGLOBINA KOD DOBROVOLJNIH DAVAOCA KRVI

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UVOD: Hemoglobin je krvni pigment, metaloprotein koji u strukturi sadrži željezo te služi za prijenos kisika.Prije svakog darivanja krvi obavezno je provjeravanje zdravstvenog stanja davaoca i vrijednosti hemoglobina u krvi.

CILJ/SVRHA: Cilj ovog istraživanja je klinička revizija kontrole mjerenja vrijednosti hemoglobina kod dobrovoljnih davaoca krvi na dva različita aparata s ciljem provjere tačnosti rezultata.

MATERIJAL I METODE: Retrospektivna analiza provedena je korištenjem podataka iz Informacionog sistema Zavoda i hematološkog analizatora za period od 2023-2026.g. Analizirane su vrijednosti i procenat odstupanja hemoglobina na aparatima iz kapilarne i venske krvi.Prikupljeni podaci su obrađeni deskriptivnom statistikom kroz numeričke i grafičke prikaze.

REZULTATI: Rađeno je poređenje vrijednosti i procenat odstupanja hemoglobina na aparatima iz kapilarne i venske krvi. Anketom su obuhvaćeni kartoni dobrovoljnih davaoca krvi registrovani u Zavodu za transfuzijsku medicine FBiH u period od 2023-2026.g. Ukupna prosječna razlika u mjerenju vrijednosti hemoglobina na dva različita aparata je minimalna.

ZAKLJUČAK: Uvidom u podatke iz kartona dobrovoljnih davaoca krvi došli smo do zaključka da vrijednosti hemoglobina na hematološkom analizatoru prikazuju minimalna odstupanja u odnosu na vrijednosti hemoglobina na aparatu za kapilarnu krv. Obzirom da se radi o dvije različite metode možemo zaključiti da su odstupanja minimalna koja ne utiču na konačni odabir prema unaprijed određenim standardima odabira davaoca prema vrijednostima hemoglobina.Najčešći razlozi u odstupanju mjerenja vrijednosti hemoglobina iz kapilarne krvi je sama osjetljivost aparata koja zavisi od pravilnog postupka pri uzrokovanju kapilarne krvi i redovnog mehaničkog čišćenja aparata.

KLJUČNE RIJEČI: dobrovoljni davaoc krvi, hemoglobin, hematološki analizator

PP 008

CLINICAL AUDIT-CONTROL OF THE MEASUREMENT OF HEMOGLOBIN VALUES IN VOLUNTARY BLOOD DONORS

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INTRODUCTION: Hemoglobin is a blood pigment, a metalloprotein that contains iron in its structure and is used to transport oxygen. Before each blood donation, it is mandatory to check the health status of the donor and the value of hemoglobin in the blood.

GOAL/PURPOSE: The aim of this research is a clinical audit of hemoglobin measurement control in voluntary blood donors on two different devices with the aim of checking the accuracy of the results.

MATERIAL AND METHODS: The retrospective analysis was carried out using data from the Information System of the Institute and the hematology analyzer for the period from 2023-2026. Values and percentage deviations of hemoglobin on devices from capillary and venous blood were analyzed. Collected data were processed with descriptive statistics through numerical and graphic displays.

RESULTS: A comparison of values and percentage deviations of hemoglobin on devices from capillary and venous blood was made. The survey included records of voluntary blood donors registered in the Institute for Transfusion Medicine of the FBiH in the period from 2023-2026. The overall average difference in the measurement of hemoglobin values on two different devices is minimal.

CONCLUSION: By examining the data from the records of voluntary blood donors, we came to the conclusion that the hemoglobin values on the hematology analyzer show minimal deviations in relation to the hemoglobin values on the capillary blood machine. Given that these are two different methods, we can conclude that the deviations are minimal and do not affect the final selection according to predetermined standards of donor selection according to hemoglobin values. The most common reasons for deviations in the measurement of hemoglobin values from capillary blood is the sensitivity of the apparatus itself, which depends on the correct procedure when causing capillary blood and regular mechanical cleaning of the apparatus.

KEY WORDS: voluntary blood donor, hemoglobin, hematology analyzer

PP 009

UČESTALOST POZITIVNOG DIREKTNOG ANTIGLOBULINSKOG TESTA KOD ZDRAVIH DOBROVOLJNIH DAVALACA KRVI U SRBIJI

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UVOD: Direktni antiglobulinski test (DAT) koristi se radi detekcije imunoglobulina i/ili komponenti komplementa vezanih za eritrocite in vivo i učestalost pozitivnog testa u populaciji dobrovoljnih davalaca krvi (DDK) smatra se niskom.
CILJ: Utvrditi učestalost pozitivnog direktnog antiglobulinskog testa u populaciji dobrovoljnih davalaca krvi i analizirati njihove kliničke i laboratorijske karakteristike.
MATERIJAL I METODE: Prospektivna studija analizirala je podatke o pozitivnom direktnom antiglobulinskom testu kod dobrovoljnih davalaca krvi u Zavodu za transfuziju krvi Vojvodine, u periodu od januara 2022. do januara 2026. godine. DAT je određen metodom u gelu, dok je kod DDK sa pozitivnim DAT-om sprovedeno određivanje monospecifičnog DAT-a, kao i kontrolnog DAT-a nakon šest meseci. Analizirana je i asocijacija pozitivnog DAT-a prema polu i starosti DDK.
REZULTATI: U studiju je uključeno 81,138 DDK, 24,342 (30%) žena i 56,796 (70%) muškaraca. Pozitivan DAT detektovan je kod 82 (0,101%) DDK, 24 (0,03%) žena i 58 (0,07%) muškaraca. Statističkom analizom nije utvrđena signifikantna razlika DAT pozitivnosti prema polu i starosti DDK. Određivanje monospecifičnog DAT-a pokazalo je većinom IgG pozitivnost (79; 96,3%), dok je pozitivan kontrolni DAT detektovan kod 56 (68,3%) DDK. Svi DDK bili su klinički zdravi, bez terapije, anemije ili hemolize.
ZAKLJUČAK: Učestalost pozitivnog DAT-a u populaciji dobrovoljnih davalaca krvi ostaje niska. Perzistiranje pozitivnog DAT-a uočeno je kod većine inicijalno DAT pozitivnih DDK, sugerišući da se pozitivan DAT svakako može odrediti i kod zdravih pojedinaca.
KLJUČNE REČI: DAT, gel metoda, davaoci krvi.

PP 009

THE INCIDENCE OF DIRECT ANTIGLOBULIN TEST POSITIVITY IN HEALTHY SERBIAN BLOOD DONORS

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Introduction: The direct antiglobulin test (DAT) is used to detect immunoglobulins and/or complement components bound to red blood cells in vivo and its incidence among healthy blood donors (BD) is considered rare.
Aim: The aim of the study was to determine the incidence of positive DAT results among healthy Serbian BD and to analyze their clinical and laboratory characteristics.
Materials and Methods: In a prospective study, the data related to positive DAT among healthy BD were analysed, from January 2022 to January 2026, at the Blood Transfusion Institute of Vojvodina. Direct antiglobulin testing was performed using gel card technology and BD with positive DAT results underwent monospecific and control DAT testing after six months. The association of DAT positivity and donor gender and age was also analysed.
Results: A total of 81,138 BD were included, 24,342 (30%) were female and 56,796 (70%) were male. Positive DAT results were detected in 82 (0,101%) BD, 24 (0,03%) were female and 58 (0,07%) were male. Statistical analysis showed no significant difference in DAT positivity according to gender and age. Most of the BD were IgG positive (79; 96,3%) while control DAT testing showed persistant positivity in 56 (68,3%) donors. All BD were clinically healthy, without medication, anaemia or haemolysis.
Conclusion: The incidence of positive DAT results in Serbian BD remains low. Persistence of DAT positivity was observed in the majority of DAT positive donors, supporting the findings that positive DAT results may occur in healthy individuals.
Keywords: DAT, gel cards, blood donors.

PP 010

"UČESTALOST POVIŠENE KONCENTRACIJE TESTOSTERONA MEĐU DOBROVOLJNIM DAVAOCIMA KRVI U VOJVODINI I POTENCIJALNI ZNAČAJ ZA BEZBEDNOST KRVI"

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Uvod: Upotreba anaboličko-androgenih steroida među dobrovoljnim davaocima krvi (DDK) predstavlja potencijalni rizik za bezbednost transfuzije zbog mogućeg prenosa transfuzijom prenosivih infekcija, prisustva steroida u krvi i policitemije korisnika. Direktno dokazivanje steroida zahteva specijalizovane analize koje nisu deo rutinske transfuzijske prakse, pa se otkrivanje zasniva na anamnestičkim podacima, kliničkom pregledu i laboratorijskim parametrima.
Cilj: Ispitati učestalost povišene koncentracije testosterona među DDK muškog pola i među njima stopu odbijenih DDK nakon rutinske selekcije, radi procene bezbednosti primenjene krvi.
Materijal i metode: Studija preseka sprovedena među 485 DDK muškog pola u Zavodu za transfuziju krvi Vojvodine. Povišena koncentracija testosterona definisana je vrednostima >28 nmol/L, analizirani su i odgovori iz upitnika za DDK, nalaz vizuelne inspekcije, krvni pritisak, puls, vrednosti hemoglobina i hematokrita.
Rezultati: Prosečna starost ispitanika bila je 38±10 godina. Povišena koncentracija testosterona potvrđena je kod 62/485 (12,78%) ispitanika. Među njima, kod 46/62 (74,19%) zabeležene su vrednosti hemoglobina >150 g/L i hematokrita >44%, značajno više u odnosu na DDK sa normalnim vrednostima testosterona ($p<0,05$). Pozitivan odgovor o korišćenju steroida navelo je 34/62 (54,83%) ispitanika, ekstremna mišićna masa registrovana je kod 27/62 (43,54%), akne, strije ili ginekomastija kod 8/62 (12,90%). Povišene vrednosti krvnog pritiska i pulsa zabeležene su kod 44/62 (70,96%) ispitanika. Isključeno je 44/485 (9,07%) DDK, 18/485 (3,71%) je prošlo rutinsku selekciju i doniralo krv.
Zaključak: Upotreba testosterona među DDK predstavlja izazov u transfuzijskoj medicini. Činjenica da je 18 ispitanika sa povišenim koncentracijama testosterona prošlo rutinsku selekciju i doniralo krv ukazuje na potrebu za unapređenjem postojećih postupaka selekcije radi povećanja bezbednosti transfuzijskog lečenja.
Ključne reči: testosteron; davaoci krvi; bezbedna krv.

PP 010

"PREVALENCE OF ELEVATED TESTOSTERONE LEVELS AMONG BLOOD DONORS IN VOJVODINA AND IMPLICATIONS FOR BLOOD SAFETY"

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Introduction: Anabolic-androgenic steroid use among blood donors (BDs) may compromise transfusion safety due to the risk of transfusion-transmissible infections, steroid presence in blood, and polycythemia. As direct steroid detection requires specialized assays not routinely performed, identification relies on medical history, clinical examination, and laboratory parameters.
Objective: To determine the prevalence of elevated testosterone levels among male BDs and assess the proportion of deferred donors after routine screening to evaluate blood safety.
Materials and Methods: A cross-sectional study included 485 male BDs at the Blood Transfusion Institute of Vojvodina. Elevated testosterone was defined as serum levels >28 nmol/L. Donor questionnaire responses, visual inspection findings, blood pressure, pulse rate, hemoglobin, and hematocrit values were analyzed.
Results: Mean age was 38±10 years. Elevated testosterone levels were found in 62/485 (12.78%) donors. Among them, 46/62 (74.19%) had hemoglobin >150 g/L and hematocrit >44%, significantly more often than donors with normal testosterone levels ($p<0.05$). Steroid use was self-reported by 34/62 (54.83%), marked muscularity was observed in 27/62 (43.54%), and acne, striae, or gynecomastia in 8/62 (12.90%). Elevated blood pressure and pulse rate were present in 44/62 (70.96%). Overall, 44/485 (9.07%) donors were deferred, whereas 18/485 (3.71%) with elevated testosterone passed routine screening and donated blood.
Conclusion: Testosterone use among BDs represents a challenge in transfusion medicine. The finding that 18 donors with elevated testosterone levels passed routine screening highlights the need to improve donor selection procedures to enhance transfusion safety.
Keywords: Testosterone; Blood Donors; Blood Safety.

PP 011

IN HOUSE METHOD FOR PREPARATION OF PLATELET RICH PLASMA

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Background: Platelet-rich plasma (PRP) is an autologous blood product with a platelet concentration 3–5 times higher than that of peripheral blood. It contains growth factors and biomolecules essential for wound healing and represents an alternative therapy in various medical fields. However, no standardized preparation protocol exists.
Aims: To evaluate the efficiency of an in-house PRP preparation method and assess the influence of age, gender, smoking status, and physical activity on platelet yield.
Methods: Whole blood (20 mL) was collected from 45 donors into sodium citrate tubes. PRP was prepared using a double-centrifugation protocol (800 rpm for 5 min, then 1200 rpm for 10 min). Final PRP volume was approximately 3 mL. Platelet counts were measured using an automated hematology analyzer (MEDONIC). Demographic and lifestyle data were recorded.
Results: Mean platelet concentration increased from 197 × 10^9/L in whole blood to 1114 × 10^9/L in PRP, corresponding to a 5–6-fold enrichment. The study included 45 participants (39 males, 6 females; mean age 41 years). Female participants showed higher PRP platelet concentrations than males (1262 vs. 1090 × 10^9/L). Comparable PRP yields were observed between smokers and non-smokers, participants with and without regular physical activity, and age groups 20–40 years and >40 years (1170 vs. 1149 × 10^9/L). No significant differences in platelet yield were observed according to age, gender, smoking status, or physical activity.
Conclusions: The in-house PRP preparation method achieved consistent 5–6-fold platelet enrichment and proved to be simple and cost-effective. Further studies are required to assess PRP quality and clinical efficacy.
Keywords: PRP; autologous blood product; regenerative medicine

PP 011

PP 012

PERZISTENTNO REAKTINI ANTI-HCV SKRINING TESTOVI KOD DAVALACA KRVI BEZ POTVRĐENE INFEKCIJE - LABORATORIJSKE I KOMUNIKACIONE DILEME

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Uvod: Skrining davalaca krvi na transfuzijom prenosive infekcije sprovodi se visokoosetljivim hemiluminiscentnim imunološkim metodama (CMIA/CLIA), ELISA metodom i molekularnim testiranjem (NAT). U populaciji niskog rizika, kakvu čine dobrovoljni davaoci krvi, uprkos visokoj specifičnosti testova dolazi do pojave lažno reaktivnih rezultata. Takvi nalazi mogu dovesti do privremene zabrane davanja krvi, dodatne dijagnostičke obrade i zabrinutosti davalaca, predstavljajući značajan laboratorijski i komunikacioni izazov.
Cilj: Analiza perzistentne reaktivnosti anti-HCV skrining testova kod davalaca bez potvrđene infekcije (negativan NAT i negativan Western blot test), procena njenog dijagnostičkog značaja i uticaja na dalji tok davanja krvi.
Materijal i metode: Sprovedena je retrospektivna analiza davalaca sa prvim reaktivnim anti-HCV rezultatom bez potvrde infekcije, kojima je određena privremena zabrana davanja krvi, a koji su se ponovo javili na donaciju u periodu 2022–2025. godine. Podaci su prikupljeni iz protokola i informacionog sistema ustanove. Testiranje je sprovedeno na platformama Architect, Alinity, Atellica, Liaison i Bio-Rad. Praćeni su rezultati ponovnog testiranja u skladu sa važećim algoritmom, ukidanje privremene zabrane i odziv davalaca na kontrolno testiranje.
Rezultati: U posmatranom periodu prikupljeno je i testirano 296.236 jedinica krvi. Privremenu zabranu davanja krvi imalo je 210 davalaca koji su donirali krv u tom intervalu. Distribucija po godinama iznosila je: 55 u 2022, 39 u 2023, 57 u 2024. i 59 u 2025. godini. Ukidanje privremene zabrane zabeleženo je kod 45,6–63,6% davalaca. Perzistentna serološka reaktivnost potvrđena je kod 103 davaoca (49%). Odziv davalaca na kontrolno testiranje nakon isteka preporučenog perioda odlaganja iznosio je svega 3%.
Zaključak: Perzistentna reaktivnost anti-HCV skrining testova bez potvrde infekcije nije redak nalaz u populaciji sa niskom prevalencijom HCV infekcije. Nizak odziv davalaca na rekontrolu dovodi do gubitka potencijalno bezbednih davalaca krvi i smanjenja raspoložive donorske baze. Sveobuhvatno tumačenje seroloških i molekularnih nalaza tokom vremena, uz ciljanu edukaciju i organizovano praćenje davalaca, predstavlja važan preduslov za očuvanje bezbednosti transfuzijskog lečenja i dugoročnu stabilnost sistema dobrovoljnog davalaštva krvi.
Ključne reči: anti-HCV test, davaoci krvi, perzistentna reaktivnost, bezbednost transfuzije

PP 012

PERSISTENTLY REACTIVE ANTI-HCV SCREENING TESTS IN BLOOD DONORS WITHOUT CONFIRMED INFECTION - LABORATORY AND COMMUNICATION DILEMMAS

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Introduction Blood donor screening for transfusion-transmitted infections is performed using highly sensitive chemiluminescent immunoassay methods (CMIA/CLIA), ELISA, and nucleic acid testing (NAT). In low-risk populations, such as voluntary blood donors, false-reactive results occur despite the high specificity of the assays. Such findings can lead to temporary donor deferral, additional diagnostic workup, and donor anxiety, presenting a significant laboratory and communication challenge.
Objective To analyze the persistent reactivity of anti-HCV screening tests in blood donors without confirmed infection (NAT-negative and Western blot-negative), and to evaluate its diagnostic significance and impact on the future course of blood donation.
Material and Methods A retrospective analysis was conducted on blood donors with an initial reactive anti-HCV result without confirmation of infection, who were placed on temporary deferral and returned for donation between 2022 and 2025. Data were retrieved from the institution's protocols and information system. Testing was performed across the Architect, Alinity, Atellica, Liaison, and Bio-Rad platforms. Follow-up criteria included re-testing results in accordance with the current algorithm, reinstatement of deferred donors, and donor compliance (response rate) regarding follow-up testing.
Results During the observed period, 296,236 blood units were collected and screened. Temporary donor deferral was applied to 210 donors who donated blood within this interval. The annual distribution was as follows: 55 in 2022, 39 in 2023, 57 in 2024, and 59 in 2025. Reinstatement (reversal of temporary deferral) was recorded in 45.6%–63.6% of donors. Persistent serological reactivity was confirmed in 103 donors (49%). The donor response rate for follow-up testing after the expiration of the recommended deferral period was only 3%.
Conclusion Persistent reactivity of anti-HCV screening tests without confirmation of infection is not an uncommon finding in a population with a low prevalence of HCV infection. The low donor response rate for re-testing leads to the loss of potentially safe blood donors and reduces the available donor pool. A comprehensive, longitudinal interpretation of serological and molecular findings, combined with targeted education and organized donor follow-up, represents an essential prerequisite for maintaining the safety of transfusion therapy and ensuring the long-term stability of the voluntary blood donation system.
Keywords: anti-HCV test, blood donors, persistent reactivity, transfusion safety

PP 013

ULOGA INSTAGRAMA U PROMOCIJI DOBROVOLJNOG DAVANJA KRVI NA PRIMERU KAMPANJE „NIŠTA BEZ ŽENA"

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Društvene mreže predstavljaju značajan kanal savremene komunikacije. Institut za transfuziju krvi Srbije (ITKS) redovno plasira promotivne kampanje putem Facebook-a, Instagram-a i Viber zajednice. Od 2025. objave na Instagramu bustovane su radi bolje vidljivosti široj populaciji. Kampanje („Jedan potez za život", „Kada život čeka ti odlučuješ", „Izvuci AS iz rukava", „Crveno je uvek IN") ostvarile su milionske preglede na mesečnom nivou. Više od 85% korisnika koji su pregledali sadržaj nisu direktni pratioci profila.
Cilj rada je analiza uticaja Instagram kampanje „Ništa bez žena" na vidljivost promotivnih aktivnosti i odziv žena dobrovoljnih davalaca krvi.
Izvršena je komparativna analiza rezultata kampanje „Ništa bez žena" 2025. i 2026. Promotivna kampanja 2025. bila je usmerena ka celokupnoj javnosti, a 2026. ciljano usmerena ka ženskoj populaciji iz Beograda starosti od 18 do 50 godina. Analizirani su podaci o broju pregleda kampanje, kao i odziv na akcije, posebno ženske populacije.
Broj pregleda Instagram kampanje „Ništa bez žena" porastao je sa 145 831 u 2025. na 623 072 u 2026. U akciji 2025. odazvale su se 153 osobe, od čega 98 žena, dok je krv dalo 129 osoba, među kojima 85 žena (65.9%). U 2026. akciji se odazvalo 210 osoba, od čega 168 žena, a krv je dala 181 osoba, uključujući 141 ženu (77.9%).
Instagram kampanje omogućavaju brzo širenje informacija, veliku vidljivost i efikasan su vid promocije koji motiviše građane da dobrovoljno daju krv. Kampanja „Ništa bez žena" pokazala je da ciljane aktivnosti uz adekvatno targetiranje populacionih grupa na društvenim mrežama mogu doprineti većem odzivu davalaca krvi.
KLJUČNE REČI: Instagram, dobrovoljno davalaštvo krvi, društvene mreže

PP 013

THE ROLE OF INSTAGRAM IN THE PROMOTION OF VOLUNTARY BLOOD DONATION - A CASE STUDY OF THE "NOTHING WITHOUT WOMEN" CAMPAIGN

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Social media represent an important channel of modern communication. The Blood Transfusion Institute of Serbia (BTIS) regularly conducts promotional campaigns through Facebook, Instagram and the Viber community. Since 2025, Instagram posts have been boosted to achieve greater visibility among the general population. Campaigns ("One Move for Life", "When Life Waits, You Decide", "Pull an Ace from Your Sleeve", "Red Is Always IN") have generated millions of views on a monthly basis. More than 85% of users who viewed the content were not direct followers of the profile.
The aim of this study was to analyze the impact of the Instagram campaign "Nothing Without Women" on the visibility of promotional activities and on the response of female voluntary blood donors.
A comparative analysis of the results of the "Nothing Without Women" campaign in 2025 and 2026 was conducted. In 2025, the promotional campaign was directed toward the general public, while in 2026 it was specifically targeted at women aged 18 to 50 living in Belgrade. Data on the number of campaign views and donor turnout were analyzed, with particular attention to the participation of women.
The number of views of the Instagram campaign "Nothing Without Women" increased from 145 831 in 2025 to 623 072 in 2026. In the 2025 campaign, 153 individuals responded, including 98 women, while 129 people donated blood, of whom 85 were women (65.9%). In the 2026 campaign, 210 individuals responded, including 168 women, while 181 people donated blood, including 141 women (77.9%).
Instagram campaigns enable the rapid dissemination of information, provide high visibility, and represent an effective form of promotion that motivates citizens to donate blood voluntarily. The "Nothing Without Women" campaign demonstrated that targeted activities, combined with appropriate audience targeting on social media can contribute to a greater response among blood donors.
KEYWORDS: Instagram, voluntary blood donation, social media

PP 014

KAMPANJA DOBROVOLJNOG DAVANJA KRVI SA MIXED REALITY NAOČARIMA

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Institut za transfuziju krvi Srbije (ITKS) kontinuirano sprovodi promotivne aktivnosti radi povećanja broja dobrovoljnih davalaca krv. Od 4. do 15. avgusta 2025. u sali ITKS realizovana je kampanja "Davanje krvi sada postaje nesvakidašnje iskustvo", zasnovana na primeni Mixed Reality (MR) naočara.
Cilj rada je prikaz efikasnosti primene MR naočara u promociji dobrovoljnog davalaštva i procena njihovog uticaja na odziv davalaca.
Priprema kampanje obuhvatila je edukaciju zaposlenih, izradu ankete za davaoce, dizajn promotivnih i video materijala, kao i medijsku promociju. Davaoci su birali između dva virtuelna okruženja (Zen Garden i Intergalactic). Sprovedena je kvalitativna analiza uvedene inovacije i analiza anketa popunjenih nakon donacije, radi poređenja iskustva sa i bez primene MR naočara. Izvršena je i komparativna analiza broja prikupljenih jedinica krvi u sali ITKS u istom periodu 2024. i 2025.
Tokom kampanje prikupljena je 1 241 jedinica krvi, što predstavlja povećanje od 10.5% u odnosu na isti period 2024. MR naočare koristilo je 395 davalaca (31.8%), dok je prvi put krv dala 301 osoba, 21.9% više nego prethodne godine. Prosečna starost davalaca koji su koristili MR naočare iznosila je 36.4 godine. U anketi 76.6% davalaca ocenilo je da je davanje krvi prijatnije uz MR tehnologiju, 81.2% davalaca ponovilo bi ovo iskustvo, a 89.3% preporučilo bi ih prijateljima. Mediji su svakodnevno izveštavali o MR tehnologiji u dobrovoljnom davalaštvu.
Upotreba digitalnih tehnologija predstavlja inovativan i efikasan pristup u promociji dobrovoljnog davalaštva. Integracija virtuelnih sadržaja povećala je motivisanost za dobrovoljno davanje. Rezultati ukazuju na potencijal šire primene sličnih tehnoloških rešenja u budućim kampanjama.
KLJUČNE REČI: inovacije, tehnologija, motivacija

PP 014

VOLUNTARY BLOOD DONATION CAMPAIGN USING MIXED REALITY GLASSES

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The Blood Transfusion Institute of Serbia (BTIS) continuously conducts promotional activities aimed at increasing the number of voluntary blood donors. From August 4 to August 15, 2025, the campaign "Blood Donation Is Now Becoming an Extraordinary Experience" was implemented at the BTIS donation center, based on the use of Mixed Reality (MR) glasses.
The aim of this study was to present the effectiveness of MR glasses in the promotion of voluntary blood donation and to assess their impact on donor turnout.
Campaign preparation included staff training, development of a donor survey, design of promotional and video materials and media promotion. Donors could choose between two virtual environments (Zen Garden and Intergalactic). A qualitative analysis of the introduced innovation was conducted, together with an analysis of surveys completed after donation, in order to compare the donation experience with and without the use of MR glasses. A comparative analysis of the number of blood units collected at the BTIS donation center during the same period in 2024 and 2025 was also performed.
During the campaign, 1 241 units of blood were collected, representing an increase of 10.5% compared with the same period in 2024. MR glasses were used by 395 donors (31.8%), while 301 individuals donated blood for the first time, which was 21.9% more than in the previous year. The average age of donors who used MR glasses was 36.4 years. In the survey, 76.6% of donors reported that blood donation was more pleasant with MR technology, 81.2% stated that they would repeat the experience, and 89.3% said they would recommend it to their friends. The media reported daily on the use of MR technology in voluntary blood donation.
The use of digital technologies represents an innovative and effective approach to promoting voluntary blood donation. The integration of virtual content increased motivation for voluntary donation. The results indicate the potential for broader implementation of similar technological solutions in future campaigns.
KEYWORDS: innovation, technology, motivation

PP 015

IDENTIFIKACIJA I KLINIČKI ZNAČAJ ANTI-P1 ANTITIJELA REAKTIVNOG NA 37 °C: OD LABORATORIJSKE DETEKCIJE DO TRANSFUZIJSKE PRAKSE – PRIKAZ SLUČAJA

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UVOD: Antigen P1 je jedini koji pripada P krvnogrupnom sistemu. Anti-P1 antitijelo je najčešće prirodno IgM antitijelo reaktivno na niskim temperaturama i uglavnom nema klinički značaj. Rijetko je reaktivno na 37 °C, kada može izazvati hemolizu transfundovanih P1 Ag pozitivnih eritrocita.
CILJ: Dokazati prisustvo anti-P1 antitijela reaktivnog na 37 °C koje je dovelo do pozitivne unakrsne probe i sporne kg.
MATERIJAL I METODE: Krvna grupa određena je automatizovanim gel-sistemom IH-500. Detekcija i identifikacija antitijela rađene su gel-karticama (LISS/Coombs i NaCl), uz DAT i IAT testove. Korišćeni su A1 i H lektini, kao i komercijalni paneli. Unakrsna proba izvedena je na 37 °C i 4 °C.
PRIKAZ SLUČAJA: Pacijentkinja S.K. (1958) hospitalizovana je zbog anemije (Hb 70 g/L). Dvadeset dana ranije primila je dvije doze DPE A RhD pozitivne krvne grupe.
REZULTATI: Krvna grupa potvrđena je kao A RhD pozitivna, uz neočekivanu aglutinaciju sa A1 eritrocitima. Fenotip pacijentkinje je CCD-ee, K-, P1-. DAT je negativan, a IAT pozitivan (2+). Identifikacija antitijela na 37 °C i 4 °C ukazala je na prisustvo aloanti-P1 antitijela, širokog temperaturnog opsega. Interreakcija sa P1 - jedinicom DPE, bila je kompatibilna.
ZAKLJUČAK: Anti-P1 antitijelo reaktivno na 37 °C ima klinički značaj zbog mogućnosti izazivanja hemolizne transfuzijske reakcije. Pravovremena identifikacija omogućava bezbjedno transfuzijsko liječenje i kvalitetnu imunohematološku dijagnostiku.
KLJUČNE RIJEČI: anti-P1 antitijelo, 37C, sporna krvna grupa

PP 015

IDENTIFICATION AND CLINICAL SIGNIFICANCE OF ANTI-P1 ANTIBODY REACTIVE AT 37 °C: FROM LABORATORY DETECTION TO TRANSFUSION PRACTICE – A CASE REPORT

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INTRODUCTION: The P1 antigen is the only antigen belonging to the P blood group system. Anti- transfused P1 antigen-positive red blood cells.
AIM: To demonstrate the presence of anti-P1 antibody reactive at 37 °C, which led to a positive crossmatch and ABO discrepancy.
MATERIALS AND METHODS: Blood grouping was performed using the automated gel system IH-500. Antibody detection and identification were carried out using gel cards (LISS/Coombs and NaCl), together with DAT and IAT testing. A1 and H lectins, as well as commercial antibody panels, were used. Crossmatching was performed at 37 °C and 4 °C.
CASE REPORT: Patient S.K. (born 1958) was hospitalized due to anemia (Hb 70 g/L). Twenty days earlier, she had received two units of A RhD-positive packed red blood cells.
RESULTS: Blood group testing confirmed A RhD positive, with unexpected agglutination with A1 red cells. The patient's phenotype was CCD-ee, K-, P1-. DAT was negative, while IAT was positive (2+). Antibody identification at 37 °C and 4 °C indicated the presence of alloanti-P1 antibody with a wide thermal range. Crossmatch testing with a P1-negative RBC unit was compatible.
CONCLUSION: Anti-P1 antibody reactive at 37 °C is clinically significant due to the potential risk of hemolytic transfusion reactions.
KEY WORDS: anti-P1 antibody, 37 °C, ABO discrepancy

PP 016

BLOOD GROUP MOLECULAR GENOTYPING WITH RT-PCR

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Blood group molecular genotyping is used to clarify problems in patient serology and screening for donors with rare blood types. An advance in this field is the non-invasive fetal RHD diagnostics in pregnancies of D-negative women to determine the fetal RHD. One of the latest molecular methods used for testing in reference centers for immunohematology is real time RT-PCR. The advantages of this molecular method are the wider range of different antigens available for typing and less time consuming.

Aim: To compare different weak serological reactions of the ABO and D antigen to the corresponding ABO, RHD genotype obtained by RT-PCR.

Material and method: Molecular ABO, RHD genotyping with two different kit reagents was performed in 40 blood donor, 33 pregnant women, 24 newborn and 36 patients who were serologically typed but with unsolved results. RT-PCR technique was used for all the samples.

Results: With RT-PCR kit reagents all unsolved and not clear results were successfully solved.

Conclusions: RT-PCR is advanced molecular genotyping which play an important role in Transfusion Medicine and provides high accuracy of results. This new genotyping strategy is required to identify correct ABO or Rh alleles. It allows donors and patients to be typed for a broad spectrum of antigens, including rare blood types, and will therefore be useful for extended antigen profiles. RT-PCR blood group genotyping will contribute making Transfusion Medicine more patient orientated.

PP 016

PP 017

DISCREPANT RESULTS IN ABO BLOOD GROUP SYSTEM IN AMBILANT PATIENTS AT THE GENERAL HOSPITAL SUBOTICA FROM 2023.-2025., WITH A CASE REPORT OF A RARE SUBGROUP „A „

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Introduction: The ABO blood group system is the most clinically important blood group system. Accurate typing of the ABO blood group system is a prerequisite for succesful and safe blood transfusion practice.
Objective: The aim of this study is to present the the discrepancies in typing the ABO blod group system, along with a case report of a patient with a rare subgroup „A".
Matherial and methods: Blood group typing using the tube method (Imunodijagnostika and Lorne), gel method with and without enzymes, and absorption and elution tests.
Results: Out of 5185 ambulant samples (2023.-2025.), we identifield 15 cases of discrepancy between antigenes on erythrocytes and the investigated antibodies in the serum. In 10 cases, an A2/A2B blood group with irregular anti -A1 antibodies was found, 4 cases of A1with alloantibodies (anti -Le a, anti-M, anti-P1). In one case, the discrepancy was due to the lack of A and B antigens, with the serum showing positivity only with known B erythrocytes. With anti -A1: neg;anti -H:3+. Using the MGS method (with and without enzymes): anti- A:neg, anti B:neg, anti -AB:neg, A1:neg, B:4+. DAT:neg.
Screening :NaCl and LissCoombs :negaive. The absorption test with anti-A,anti-B,and anti-AB serum showed a decrease in titer with anti-AB serum from 1/2048 to 1/512, while anti-A and anti-B there was no reduction. Heat elution test: titer with anti-A:neg, with enzim ½, titer with antiB:neg, titer with anti -AB :neg, with enzyme ½. Conclusion: weak A subgroup, with suspicion of Ay. The sample was sent to the ITK Serbia, where molecular typing comfirmed that the individual is a homozygote for the ABO*01 allele and a rare ABO subgroup.
Conclusion: from 1964. to 1995. the patient was a voluntary blood donor. Until 1974. (in house serums) she was registred as ORhDneg, and from 1974. (commercial serums) as A3. This case demonstrates how the development of serum quality and technology improves the quality of work.

PP

PP 018

RH D NEGATIVE PREGNANT WOMAN WITH ASSOCIATION OF ANTI-D AND ANTI-C ALLOANTIBODIES THE MOST IMPORTANT MATERNO-FETAL INCOMPATABILITY IS IN THE RHESUS SYSTEM : D, C, C, E, E.

Galina Genova

Our case is Rh D negative pregnant woman with anti-D and anti-C antibodies in 16 weeks gestation. We did screening, identification and titration of the antibodies in two methods (IAT and enzymatic test), extended phenotype of the father and the newborn and determination of IgG subclasses to assess the clinical significance of the red cell alloantibodies.The titer of anti- D antibody increased from 128 to 1024. Anti- C antibody was detected only in enzyme technique and was considered clinically insignificant in terms of HDFN. The newborn was with positive DAT and ongoing hemolysis on the 5th day of birth.
We should implement adsorbtion and elution test procedure to differentiate anti-D+C and anti-G and IH-500 titration procedure to optimise our laboratory practice.
HDFN, pregnancy, alloantibodies, screening, identification, titration.

PP

PP 019

RED BLOOD CELL ALLOIMMUNIZATION IN PREGNANT WOMEN IN THE REPUBLIC OF NORTH MACEDONIA

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Introduction: The risk of developing hemolytic disease of the fetus and newborn (HDFN) in alloimmunized pregnant women depends on the specificity and titer of maternal antibodies, as well as the presence of the corresponding red blood cell antigen in the fetus. Early detection of clinically significant antibodies is essential for timely risk assessment and reduction of perinatal morbidity and mortality.
Objective: To determine the prevalence and specificity of red blood cell alloantibodies among pregnant women in the Republic of North Macedonia.
Materials and Methods: A retrospective study was conducted at the Institute of Transfusion Medicine of the Republic of North Macedonia from June 2022 to June 2024. A total of 5623 pregnant women were screened. Antibody detection and identification were performed using the indirect antiglobulin test in gel microcolumns (ID-Card LISS/Coombs) on the IH-500 automated system (Bio-Rad).
Results: Red blood cell alloantibodies were detected in 2.53% (142/5623) of women. Rh antibodies were identified in 1.73%, while antibodies against other blood group systems were found in 0.44%. Anti-D was the most prevalent antibody (56.34%), followed by anti-M (6.34%), anti-E (5.63%), and anti-K (3.52%). Less common antibodies included anti-C, anti-c, anti-Fyb, anti-S, anti-Lea/Leb, anti-Cw, and anti-Jka. Antibodies of undetermined specificity were detected in 0.32% of women.
Conclusion: Rh antibodies, particularly anti-D, remain the predominant cause of red blood cell alloimmunization in pregnancy. Universal antenatal antibody screening is essential for the early identification of high-risk pregnancies and prevention of severe HDFN and adverse perinatal outcomes.
Keywords: red blood cell alloimmunization, pregnancy, alloantibodies, hemolytic disease of the fetus and newborn (HDFN), Rh blood group system, anti-D, antenatal screening.

PP

PP 020

MANAGEMENT OF ANTI-M ANTIBODY DURING PREGNANCY - CASE REPORT

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Background: Anti-M is a relatively common naturally occurring antibody reacting optimally at 4°C and weakly or nonreactive at 37°C. It is usually clinically insignificant but can be active at 37°C because of thermal amplitude of IgM component or presence of IgG component. Alloimmunization due to anti-M antibodies are rare since IgM antibodies do not cross the placenta. Very rarely, these may convert to immunoglobulin G antibodies and cause hemolytic disease of the fetus and newborn. We present the case of a gravida, with previous miscarriage, booked with us the 12 week of pregnancy for Indirect Antiglobulin Test (IAT).
Objective: To review the general guidelines and propose a less intensive management approach of anti-M antibody during pregnancy through the context of a case report.
Methods: We report a 32-year-old pregnant woman presenting for antepartum care. She was found to have a positive IAT, and with further testing was identified anti-M antibody, active at 37°C, IgG class. The antibody titer was being monitored serially and was stable at 1:64 throughout pregnancy. At 37 weeks titer got 1:128 and in consultation with gynaecologist she was prepared for delivery.
Results: She birthed a healthy-term infant, at 37+5 weeks without complications. The baby had no signs of heamolysis and anemia, and no therapy was needed.
Conclusion: Anti-RBC antibodies, including anti-M, are frequently identified in blood type and screening for pregnant patients. Guidelines call for intensive surveillance during pregnancy; however, knowledge of the specific antibody can help to provide more nuanced and less intensive care. The maternal antibody titers may not be a true reflection of the severity of fetal affection.
Keywords: alloimunization, anti-M antibodies, HBNF

PP

PP 021

THE ROLE OF ABO BLOOD GROUP SYSTEM IN THE OCCURRENCE OF VENOUS THROMBOEMBOLISM

Background. The association of blood group antigens, especially those from the ABO system and some diseases is well known. The alleles of the ABO locus have functional effect on the level of some plasma coagulation factors which contributes to a thrombophilic condition and increase the risk for occurrence of venous thromboembolism.
Aim. To examine relationship between ABO blood genotype with the occurrence of thromboembolic disease in our population, as well as to asses the risk for thrombosis in individuals with non-OO blood group genotype in comparison to those who poses it. To examine relationship between ABO blood group genotype and and genetic thrombophilic markers with the occurrence of venous thromboembolism.
Material and methods. This prospective case control study included 52 patients with a confirmed diagnosis of venous thromboembolism (VTE) and a control group of 50 healthy subjects who do not have a personal or family history of thrombosis. The tests were performed on a sample of venous blood 2-6 ml in EDTA. In addition to the serological ABO typing, ABO aleles from ABO system (A1, A2, O1, O2, B) were determined by molecular methods (PCR-SSP and RT-PCR). Thrombophilia markers (factor II G20210A, factor V Leiden G1691A, factor XIII V34L: c 103 G>T, factor VII G10976A, FGB 455 G/A, MTHFR C677: c 665 C>T, MTHFR A1298c: c 1298 A>C, MTR A2756G, MTRR A66G, PAI-1 5G/4G) were determinate by molecular methods (RT-PCR) in patients with confirmed VTE.
Results. The results from ABO phenotyping and ABO genotyping performed in patients with VTE, as well as in the control group, show significant correlation with non-OO genotypes and occurrence of VTE in our population, in manner of increased additional trombotic risk, as a result of ABO system. Patients with VTE with non-OO genotype are with significant higher prevalence with 86.5%, in comparison with 13.5% occurrence of OO genotypes (x 2 test p=0,027 ($p<0.05$)). The most frequent genotype in group of patients with VTE is O1A1 with 40.4%, while in control group is O1O1 with 32% occurrence. The genotype O1A1 is most frequent genotype in three groups of patients with VTE, in group of patients with deep vein thrombosis (DVT), pulmonary embolism (PE) and in those where is diagnosed DVT and PE in the same time, with occurrence of 35.7%, 55.5% and 50% respectively, but with significant lower occurrence of this genotype in control group with 24%. Genotype A1A1 has statistically significant correlation with occurrence of PE in our population. In correlation with occurrence of DVT are O1A1 and O1B genotypes and in correlation with PE is O1A1 genotype. Significant correlation on PAI-1 5G/4G polimorphism with occurrence of VTE, as well as FII G20210A mutation with occurrence of DVT and PE in our population. Patients with non-OO genotypes have the biggest occurrence of polimorphisms from methylfolate metabolism (MTR, MTRR, MTHFR C677T and MTHFR A1298C) with 38.5% occurrence and with application on Pearson correlation ($p<0.05$) is confirmed statistically significant correlation on this polymorphisms with the occurrence of VTE. In statistically significant correlation with PE are obesity [body mass index (BMI≥30kg/m 2)] and metabolic syndrome, while with DVT in statistically significant correlation is arterial hypertension. As well as in correlation with DVT are some comorbidities such as hepatic, renal and respiratory diseases.
Conclusion. The results confirm association on ABO blood group system with the occurrence of venous thromboembolism, so non-OO genotypes are connected with higher trombotic risk in comparison with OO genotypes in population in R.N. Macedonia.
Keywords: ABO genotype, ABO alleles, ABO system, venous thromboembolism (VTE), deep vein thrombosis (DVT), pulmonary embolism (PE), thrombophilia.

PP 021

PP 022

HEMOLYTIC DISEASE OF THE FETUS AND NEWBORN(HBFN): DIAGNOSTIC CHALLENGES IN A CASE WITH NEGATIVE SEROLOGICAL FINDINGS

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Introduction Hemolytic disease of the fetus and newborn is an immune-mediated condition caused by maternal antibodies directed against fetal red blood cell antigens. Early recognition and appropriate laboratory evaluation are essential for timely treatment and prevention of severe neonatal complications.
Objective To present a case of newborn referred for exchange transfusion evaluation despite negative serological findings suggestive of immune hemolysis.
Materials and Methods Pretransfusion testing was performed od blood samples obtained from the mother and newborn. ABO/RhD blood grouping, indirect antiglobulin testing (IAT), direct antiglobulin testing(DAT), red blood cell phenotyping, and compatibility testing were carried out using gel microcolumn agglutination techniques. Results The mother and newborn were both identified as blood group B, RhD positive. Maternal antibody screening (IAT) was negative, while DAT performed on three separate neonatal samples was repeatedly negative. Red blood cell phenotyping revealed a maternal phenotype of C+c+E-e+K- and a neonatal phenotype of C+c-E-e+K-. Compatibility testing between the neonatal sample and the selected donor red blood cell unit showed no incompatibility. The laboratory investigation did not demonstrate evidence of alloimmune HBFN. However, the clinical indication for exchange transfusion emphasized the need for further evaluation of alternative causes of neonatal hyperbilirubinemia and anemia.
Conclusion Negative DAT and IAT results do not completely exclude clinically significant hemolysis in newborns. Comprehensive diagnostic assessment is necessary to identify both immune and non-immune causes of hyperbilirubinemia and anemia, ensuring appropriate transfusion management and avoiding unnecessary exchange transfusion procedures.
Keywords: hemolytic disease of fetus and newborn HDFN, exchange transfusion, direct antiglobulin test, neonatal hyperbilirubinemia

PP 022

PP 023

THE CONNECTION BETWEEN THE AB0 BLOOD GROUP SYSTEM AND THROMBOSIS CAUSED BY THE SARS VIRUS

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INTRODUCTION Deep vein thrombosis is a major public health problem. Blood groups of the AB0 system in combination with risk factors (smoking, obesity, poor eating habits, lack of physical activity, immobilization), genetic mutations, age and COVID infection are associated with increased predisposition and risk of thrombosis.
People of the A, B and AB blood group (not 0 blood group) have a 40 percent higher risk of thrombosis than 0 blood group and 25-30 percent higher level of Von Willebrand factor glycoprotein in the plasma.
THE GOAL OF THE WORK (AIM) To show that there is an increased risk for venous thrombosis of people suffering from SARS COVID virus blood group A, B and AB (not 0 blood group) of the AB0 blood group system compared to 0 blood group.
MATERIAL AND METHODS The protocols of the coronary units of the General hospitals of Bar and Kotor and the Blood Transfusion Institute of Montenegro were used.
WORK RESULTS Out of 2075 patients with covid, 415 patients had venous thrombosis: A blood group 162 (39%), B blood group 116 (27,9%), 0 blood group 95 (22,9%) and AB 42 (10,2%). No 0 blood group (A, B, AB) had 320 patients (77,1%) and 0 blood group 95 (22,9%). In the general population and general hospital Kotor 0 blood group is 35%, B blood group 14%, A blood group 44% and AB 7%. Among the patients in the COVID wards, there are 816(39,3%) A blood group, B blood group 575 (27,7%), 0 Blood group 481(23,2%) and AB 203(9,8%).
CONCLUSION The results of the research confirmed the association of the risk of thrombosis in people of blood groups A,B,AB (non O blood group)
Key word :ABO blood groups ,thrombosis,COVID

PP 023

PP 024

ISPITIVANJE SEROLOŠKE SLABE EKSPRESIJE D ANTIGENA KOD PACIJENATA: PRIKAZ SLUČAJA

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Uvod: Laboratorije su prešle sa tradicionalnog serološkog testiranja u epruvetama na mikrokolonsku aglutinaciju (gel) i tehnologije čvrste faze. Ove osetljivije metode mogu da detektuju slabu ekspresiju D varijanti koje bi u prošlosti bile označene kao RhD negativne. Najbolji pristup rešavanju neslaganja je molekularna analiza. Genotipizacija identifikuje tačne *RHD* alele, što precizno predviđa prisustvo delimičnih ili slabih D varijanti.
Cilj: Utvrditi status D antigena kod pacijenata sa serološki slabom ekspresijom D antigena, korišćenjem seroloških i molekularnih tehnika.
Materijal i metode: Analizirani su uzorci krvi četiri pacijenta kod kojih serološkim metodama nije bilo moguće jasno odrediti RhD status. Inicijalno testiranje izvedeno je anti-D IgM reagensima metodom u gelu i epruveti. Uzorci sa jačinom aglutinacije 0–2+ dodatno su testirani indirektnim antiglobulinskim testom (IAT) korišćenjem monoklonskih anti-D IgG reagensa. Direktni antiglobulinski test (DAT) i Rh fenotipizacija određeni su standardnim gel metodama. Molekularno testiranje sprovedeno je kod DAT pozitivnih ili negativnih uzoraka sa IAT reakcijom ≤3+.
Rezultati: Kod tri pacijenta zabeležene su slabe do umerene reakcije aglutinacije serološkim testovima, uz negativan DAT. Molekularnim testiranjem kod tri pacijenta potvrđen je D weak tip 1 sa Rh fenotipom Ccee. Kod jednog pacijenta dobijene su jake reakcije aglutinacije (4+ u gelu; 3+ u epruveti) dodatnim IAT testom, zbog čega molekularno testiranje nije bilo indikovano, a pacijent je klasifikovan kao RhD-pozitivan.
Zaključak: Kod serološki slabih D fenotipova preporučuje se određivanje *RHD* genotipa radi precizne klasifikacije RhD statusa. Na osnovu genotipa, pacijente je potrebno adekvatno klasifikovati kao RhD-pozitivne ili RhD-negativne, čime se omogućava pravilno transfuzijsko lečenje i primena Rh-imunoprofilakse.
Ključne reči: antigeni krvnih grupa, određivanje krvnih grupa i interreakcija, serološki testovi, molekularno-dijagnostičke tehnike.

PP 024

INVESTIGATION OF SEROLOGICAL WEAK EXPRESSION OF D ANTIGEN IN PATIENTS: CASE REPORT

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Introduction: Laboratories have moved from traditional serological tube-based testing to microcolumn agglutination (gel) and solid-phase technologies. These more sensitive methods can detect weak-expression of D variants that would have been labeled as RhD negative in the past. The best approach to resolving discrepancies is molecular analysis. Genotyping identifies the exact *RHD* alleles which accurately predicts the presence of partial or weak D variants.
Aim: To resolve D antigen status in patients with serologically weak D antigen expression, using serological and molecular techniques.
Material and methods: We analyzed four blood samples of patients with inconclusive serological RhD typing. Initial testing was performed using anti-D IgM reagents by gel and tube methods. Samples showing agglutination strength of 0–2+ were further tested by the indirect antiglobulin test (IAT) using monoclonal anti-D IgG reagents. Direct antiglobulin testing (DAT) and Rh phenotyping were performed using standard gel techniques. Molecular testing was conducted in DAT-positive or negative samples with IAT reactivity ≤3+.
Results: Three patients showed weak to moderate agglutination reactions in serological testing, with negative DAT results. Molecular analysis confirmed D weak type 1 with Rh phenotype Ccee in all three patients. One patient showed strong agglutination reactions in additional IAT testing (4+ in gel; 3+ in tube); therefore, molecular testing was not indicated, and the patient was classified as RhD-positive.
Conclusion: *RHD* genotyping is recommended in cases of serologically weak D phenotypes to ensure accurate RhD classification. Based on the genotype, patients should be appropriately classified as RhD-positive or RhD-negative, enabling optimal transfusion management and appropriate Rh immunoprophylaxis.
Keywords: Blood Group Antigens, Blood Grouping and Crossmatching, Serologic Tests, Molecular Diagnostic Techniques.

PP 025

PRIKAZ SLUČAJA: KRATKOTRAJNA PRISUTNOST“ANTI-M-LIKE ANTITELA”

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Uvod Određivanje krvnih grupa u ABO sistemu predstavlja najznačajniji test u imunohematološkoj laboratorijskoj praksi. Razrešavanje neusaglašenosti u testiranju predstavlja veliki profesionalni izazov za imunohematološku laboratoriju.
Cilj rada je prikaz retkog slučaja u kojem je detektovano i dokazano kratkotrajno prisustvo „anti-M-like” antitela koje je dovelo do diskrepance u ABO sistemu.
Materijal i metode Korišćene metode u epruveti sa test serumima “Lorne” i “CE Imunodijagnostika”; MGS metoda
Prikaz slučaja U laboratoriju je primljen uzorak krvi deteta uzrasta 14 meseci, u sklopu preoperativne pripreme za planiranu tonzilektomiju. Inicijalno krvna grupa u ABO/RH sistemu rađena je metodom u epruveti, korišćeni su monoklonski test-serumi IgM klase (Lorne i CE Imunodijagnostika) za određivanje antigena i dobijeni su sledeći rezultati: anti-A: 4+; anti-B: neg.; anti-AB:4+; anti-D:4+; sa test eritrocitima: A1:1+; B:2+ Testiranje je nastavljeno MGS tehnikom (Bio-Rad DiaClon ABO/D+Reverse Grouping): anti-A:4+, anti-B:neg., anti-D:4+, A1erci:1+, Berci:2+; podgrupa: anti-A1:4+, anti-H- / negativ/. Sc: DiaCell I 1+, II neg, III 2+ (22°C i 37°C). ID: anti-M antitelo (DiaPanel Bio Rad); DAT: Negativan; Autokontrola: Negativna. Krvna grupa: A1 RhD(+)pozitiv, MN, ccEe. Testovi kompatibilnosti MGS metodom sa A RhD+ ercitrocitima NN:negativan, MN:2+, MM:3+ Proveren imunohematološki status nakon 18 meseci kada je sc antitela bio negativan.
Zaključak: Kod prikazanog pacijenta je, usled čestih inflamatornih procesa, i stimulacije imunskog sistema, došlo do stvaranja „anti-M-like” antitela. Ovo antitelo se in vitro u testovima kompatibilnosti vezivalo za M antigen na eritrocitima davalaca dok nije pokazivalo afinitet prema sopstvenim eritrocitima (negativan DAT; autokontrola). Njegovo potpuno iščezavanje nakon 18 meseci potvrđuje da je imalo prolazan karakter.

PP 025

CASE REPORT: TRANSIENT PRESENCE OF AN “ANTI-M-LIKE” ANTIBODY

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Introduction ABO blood typing represents the most significant test in immunohematology laboratory practice. Resolving testing discrepancies represents a major professional challenge for an immunohematology laboratory.
Objective The aim of this report is to present a rare case in which the transient presence of an “anti-M-like” antibody was detected and proven, leading to a discrepancy in the ABO system.
Material and methods The tube method using “Lorne” and “CE Immunodiagnostics” test sera; MGS (Microgel System) method.
Case report A blood sample from a 14-month-old child was received by the laboratory as part of the preoperative preparation for a planned tonsillectomy. Initially, blood typing in the ABO/RhD system was performed using the tube method. Monoclonal IgM class test sera (Lorne and CE Immunodiagnostics) were used for antigen determination, yielding the following results: anti-A: 4+; anti-B: negative; anti-AB: 4+; anti-D: 4+; with test red blood cells (RBCs): A1: 1+; B: 2+. Testing was continued using the MGS technique (Bio-Rad DiaClon ABO/D+Reverse Grouping): anti-A: 4+, anti-B: negative, anti-D: 4+, A1 RBCs: 1+, B RBCs: 2+; subgroup: anti-A1: 4+, anti-H: negative. Antibody screening (Sc): DiaCell I 1+, II negative, III 2+ (22°C and 37°C). Antibody identification (ID): anti-M antibody (DiaPanel Bio-Rad); DAT: negative; Autocontrol: negative. Blood type: A1 RhD positive, MN, ccEe. Compatibility tests using the MGS method with A RhD positive RBCs: NN: negative, MN: 2+, MM: 3+. The immunohematological status was checked after 18 months, at which time the antibody screening was negative.
Conclusion: In this patient, due to frequent inflammatory processes and immune system stimulation, the formation of an “anti-M-like” antibody occurred. In vitro compatibility tests showed that this antibody bound to the M antigen on donor red blood cells, while showing no affinity towards autologous red blood cells (negative DAT; negative autocontrol). Its complete disappearance after 18 months confirms its transient nature.

PP 026

IZAZOVI U ZBRINJAVANJU PACIJENATA SA ANTI–GPIV(CD36) ANTITIJELIMA:PRIKAZ SLUČAJA.

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Uvod: Aloimunizacija na trombocitne antigene najčešće je usmjerena protiv HPA-1 i HPA-5 sistema.Međutim,CD36 je relativno nedavno definisan sistem krvnih grupa(od strane ISBT-a u maju 2024.godine).Antitijela usmjerena protiv ovog glikoproteina(GPIV)predstavljaju specifičan entitet,karakterističan za osobe sa tipom I ili II CD36 deficijencije,što može dovesti do refraktarnosti na transfuziju trombocita ili fetalne/neonatalne aloimune trombocitopenije(FNAIT).
Cilj: Prikazati dijagnostički i terapijski izazov kod pedijatrijskog pacijenta sa detektovanim anti-GPIV antitijelima,kod kojeg nije bilo moguće sprovesti molekularnu genotipizaciju niti obezbijediti kompatibilnog donora trombocita.
Materijal i metode: Pacijent pedijatrijskog uzrasta je tokom januara 2026. godine u dva navrata liječen transfuzijama ozračenih,puliranih koncentrata trombocita.Zbog sumnje na imunološku refraktarnost,uzorak krvi je testiran na prisustvo antitijela.Primijenjena je tehnika čvrste faze sa mikrosferama na Luminex platformi za skrining klinički najznačajnijih antitrobocitnih i anti-HLA antitijela.
Rezultati: Luminex metodom detektovana su specifična aloantitijela protiv glikoproteina IV(anti-GPIV),dok je rezultat bio negativan za glikoproteine GPIIb-IIIa,GPIb/IX,GPIa-IIa,kao i za HLA klasu I.Komercijalni kitovi za genotipizaciju nisu imali mogućnost otkrivanja gena odgovornog za ekspresiju CD36 antigena,te deficijencija nije molekularno potvrđena.Zbog visoke učestalosti GPIV antigena u populaciji i odsustva adekvatnog registra,podudaran donor nije mogao biti pronađen.Postavlja se pitanje da li je aloimunizacija bila preegzistentna ili indukovana januarskim transfuzijama.
Zaključak: Detekcija anti-GPIV antitijela zahtijeva visok stepen kliničke sumnje i sofisticiranu laboratorijsku dijagnostiku.Ovaj slučaj naglašava potrebu za proširenjem panela za genotipizaciju trombocitnih antigena u rutinskoj praksi i ukazuje na hitnost uspostavljanja registra rijetkih donora krvi i komponenata krvi radi adekvatnog zbrinjavanja senzibilisanih pacijenata.
Ključne riječi:anti-GPIV,CD36,trombocitna antitijela,refraktarnost,aloimunizacija.

PP 026

PP 027

„TIHA“ MAJČINA ANTIERITROCITNA AUTOANTITELA KOD NOVOROĐENČETA: PRIKAZ TRANSPLACENTARNOG PRENOSA I DETEKCIJE U MAJČINOM MLEKU

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Uvod: „Tiha” antieritrocitna autoantitela (TAERAAT) predstavljaju antitela protiv sopstvenih antigena eritrocita, koja se otkrivaju pozitivnim direktnim antiglobulinskim testom (DAT), bez pojave hemolizne anemije. TAERAAT mogu biti prisutna kod trudnica, zdravih davalaca krvi i osoba sa autoimunim poremećajima.
Cilj: Prikazujemo novorođenče kod kojeg su antieritrocitna autoantitela pasivno preneta putem placente i otkrivena u majčinom mleku.
Materijal i metode: Krv majke i novorođenčeta, kao i uzorak majčinog mleka, analizirani su imunohamatološkim metodama.
Rezultati: Žensko novorođenče rođeno u 36. gestacijskoj nedelji carskim rezom od 38-godišnje majke kod koje su **„**topla” antieritrocitna autoantitela prvi put otkrivena tokom prethodne trudnoće. Trećeg dana života registrovana je blaga anemija (hemoglobin 11,1 g/dL), bez znakova infekcije, hemolize ili gubitka krvi. Po prijemu u tercijarnu ustanovu šestog dana života, vrednosti hemoglobina iznosile su 10,4 g/dL, hematokrita 0,304 L/L, uz normalan broj retikulocita i vrednosti bilirubina.
Majka i novorođenče su krvne grupe B RhD pozitivne, CcDee, K negativni, sa pozitivnim DAT i indirektnim antiglobulinskim testom. Identifikacija antitela pokazala je panaglutinaciju uz pozitivne autokontrole iz uzoraka krvi majke i novorođenčeta. Isti obrazac reaktivnosti utvrđen je i u uzorku majčinog mleka, dok je elucija sa eritrocita novorođenčeta bila negativna.
Novorođenče je otpušteno u dobrom opštem stanju, ali je nedelju dana kasnije ponovo hospitalizovano zbog pogoršanja anemije (hemoglobin 8,8 g/dL) i retikulocitoze (3,07%). Transfuzija jedne jedinice najmanje inkompatibilnih eritrocita protekla je bez komplikacija i dobro je podneta.
Zaključak: Ovaj slučaj potvrđuje pasivni prenos majčinih TAERAAT putem placente i mleka, ukazujući na njihovu moguću ulogu u nastanku neonatalne anemije i potrebu za daljim istraživanjima.
Ključne reči: “tiha” antieritrocitna autoantitela, majčino mleko, novorođenče

PP 027

„TIHA“ MAJČINA ANTIERITROCITNA AUTOANTITELA KOD NOVOROĐENČETA: PRIKAZ TRANSPLACENTARNOG PRENOSA I DETEKCIJE U MAJČINOM MLEKU

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Ključne reči: “tiha” antieritrocitna autoantitela, majčino mleko, novorođenče

PP 028

TEŠKA HEMOLITIČKA POSTTRANSFUZIJSKA REAKCIJA IZAZVANA ANTI-"C" ALOANTITELOM

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UVOD-Posttransfuzijske reakcije predstavljaju značajnu komplikaciju transfuzijskog lečenja i najčešće su posledica imunološke reakcije primaoca na eritrocitne antigene davaoca. Poseban klinički značaj imaju odložene hemolitičke posttransfuzijske reakcije, koje su izazvane prisustvom imunih eritrocitnih aloantitela. Antitela Rh sistema, naročito anti-c antitelo, spadaju u česte uzročnike ovih reakcija i ubrajaju se u klinički značajna antitela koja mogu dovesti do izražene hemolize, posebno kod prethodno imunizovanih pacijenata. Pravovremena identifikacija aloantitela i primena fenotipski kompatibilnih krvnih komponenti imaju ključnu ulogu u prevenciji transfuzijskih komplikacija.
PRIKAZ SLUČAJA-U ovom radu prikazujemo slučaj pacijentkinje kod koje je osam sati nakon transfuzije došlo do teške odložene hemolitičke posttransfuzijske reakcije sa razvojem multiorganskih poremećaja, izazvane anti-c aloantitelom.
DISKUSIJA- Prikazani slučaj predstavlja tipičan primer anamnezične imunološke reakcije kod prethodno imunizovane pacijentkinje. Transfuzija eritrocita fenotipa CcDDee kod pacijentkinje fenotipa CCDDee rezultirala je izloženošću c antigenu, što je dovelo do imunološki posredovane hemolize sa sistemskim komplikacijama, uključujući oštećenje jetre, bubrega i poremećaj koagulacije. Ovaj slučaj dodatno naglašava značaj proširenog eritrocitnog fenotipiziranja i individualizovanog izbora krvnih komponenti kod pacijenata sa anamnezom višestrukih transfuzija.
ZAKLJUČAK- Teške odložene hemolitičke posttransfuzijske reakcije mogu se javiti i pored urednog pretransfuzionog skrininga. Ovaj slučaj ukazuje na potrebu razmatranja preventivnog proširenog fenotipiziranja (Rh, Kell) kod pacijenata sa hroničnim anemijama i planiranim ponovljenim transfuzijama.

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PP 029

HEMOLYTIC DISEASE IN THE FETUS AND NEWBORN, UNSPECIFIED

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Introduction: HBFN is a clinical syndrome that may represents a neonatal emergency, particularly concerning the Rh system (anti-E, anti-c) in an alloimmunized mother, against the fetal erythrocyte antigen. The condition is characterized by the destruction of fetal or neonatal erythrocytes through hemolysis. Treatment involves immunohematological tests and transfusiological examinations.
Goal: Diagnosis and treatment of HBFN. Promptly eliminate the cause of anemia and bilirubinemia.
Materials and methods: A 12-day-old newborn, born at 38 weeks of gestation, hospitalized at Health Center – Bitola, with pale skin and anemia: Hb=68 g/l, Hct=19.4%. Due to the lack of filtered erythrocytes, referred to the Clinical Center Skopje. BW=3790g, APGAR 8/9, developed jaundice. Due to increased GGT (gamma-glutamyl transferase), prescribed: Ursophalk.
Due to a positive DAT, additional immunohematological analyses were performed on the mother's sample. Screening tests for anti-erythrocyte antibodies: Enzyme test +, IAT +; Identification on AEAT 37°C = anti-E antibody, Enzyme identification = anti-E+c antibodies. Positive E+c antigen typing (confirms alloimmunization to anti-E and anti-c). Anti-E+c alloantibodies were identified. E+c antigen typing was performed for the given blood units (CM negative).
Discussion: In a three-week-old newborn during the period 08-09/01/26, a transfusion of filtered red blood cells was administered in accordance with the blood count (100 ml + 150 ml) filtered RBC without BC in SAGM-5.
Outcome: increase in Hb from 65 g/L to 173 g/L.
Conclusion: A positive and prompt approach in treatment is always a joint solution within the protocol for treating anemia and bilirubinemia.
Keywords: HBFN, anemia, anti-E+c alloantibodies, and filtered erythrocytes.

PP 029

PP 030

EVALUATING ERYTHROCYTE TRANSFUSION UTILIZATION AND THE NEED FOR IMPLEMENTATION OF PATIENT BLOOD MANAGEMENT IN A REGIONAL HOSPITAL IN NORTH MACEDONIA

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Background Blood transfusion remains a critical, life-saving intervention in modern healthcare; however, increasing evidence indicates that liberal or non-indicated transfusion practices may expose patients to avoidable risks, contribute to adverse outcomes, and place a significant burden on limited blood resources. Patient Blood Management (PBM) is internationally recognized as a standard of care aimed at optimizing transfusion practices through evidence-based, patient-centered strategies.

Aim To evaluate erythrocyte concentrate (EC) transfusion practices at Clinical Hospital Shtip over a four-year period and to determine the necessity for structured implementation of PBM strategies in routine clinical practice.

Methods A retrospective observational study was conducted using data from the electronic transfusion database (e-Delphyn system), hospital electronic medical records, and institutional transfusion documentation. All EC units issued between 2022 and 2025 were analyzed. Parameters included departmental distribution, transfusion indications, pretransfusion hemoglobin levels, frequency of single-unit transfusions, and donor activity trends.

Results A total of 10,280 EC units were issued during the study period. Annual utilization remained relatively stable: 2,576 units in 2022, 2,555 in 2023, 2,735 in 2024, and 2,414 in 2025. Donor activity demonstrated a steady increase from 4,625 donors in 2022 to 5,517 in 2025. Internal Medicine department accounted for the highest proportion of transfusions (45.4%), followed by Orthopedics (32.2%), Surgery (17%), and Gynecology and Obstetrics (11.3%). The mean pretransfusion hemoglobin level was approximately 8 g/dL, while 84% of transfusions were administered above the widely recommended restrictive threshold of 7 g/dL. Single-unit transfusions represented 64.6% of all transfusion episodes.

Conclusion

This study highlights a significant opportunity to align transfusion practice with current evidence-based recommendations. The high proportion of erythrocyte transfusions administered above restrictive hemoglobin thresholds suggests considerable potential for optimization through structured Patient Blood Management (PBM) strategies. Implementation of PBM principles, including standardized transfusion thresholds, proactive anemia management, clinician education, and continuous quality monitoring, may contribute to improved patient outcomes, reduced exposure to unnecessary transfusions, and more efficient utilization of blood resources. In addition to its clinical benefits, PBM has consistently demonstrated economic value, with studies from European healthcare systems reporting reduced blood utilization, shorter hospital stays, and overall cost savings following implementation. Evidence from large PBM programs has shown reductions in blood product use of up to 40% and significant healthcare savings, supporting PBM as both a clinically effective and cost-efficient strategy**. These findings support the integration of PBM into routine clinical practice and highlight its importance for improving the quality, safety, and sustainability of transfusion medicine in regional healthcare settings.**

Keywords: Patient Blood Management; Blood Transfusion; Erythrocyte Concentrate; Hemoglobin Threshold; Restrictive Transfusion Strategy; Blood Donors.

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PP 031

EVALUATION OF BLOOD UTILIZATION EFFICIENCY IN A SPECIALIZED HOSPITAL FOR NEPHROLOGY IN STRUGA, NORTH MACEDONIA

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INTRODUCTION: Blood transfusion is an invaluable therapeutic intervention, particularly in surgery, malignancies, and chronic diseases. The growing demand for blood—driven by advances in surgical procedures, aging population, and increasing cancer incidence—highlights the importance for efficient blood utilization. However, precautionary crossmatching, especially for elective surgery, often results in over-ordering, reducing availability of blood units and increasing wastage and financial burden. Quality indicators such as the crossmatch-to-transfusion ratio (CTR), transfusion probability (TP), transfusion index (TI), and utilization rate (UR) are widely used to assess blood ordering practices.

AIM: To assess blood utilization efficiency using standard transfusion indices and compare practices between medical and surgical departments.

MATERIALS AND METHODS: A retrospective review of data from the transfusion medicine department at the Specialized Hospital for Nephrology and Hemodialysis – Struga, for 2025. Crossmatch requests were obtained from registers and electronic records. CTR, TP, TI, and UR were calculated using MS Excel.

RESULTS: A total of 659 crossmatch requests were recorded: 545 from nephrology and 114 from urology department. A total of 634 units were transfused. The overall CTR was 1.04 (medical 1.003; surgical 1.252). TP was 91.1% overall, with markedly higher values in nephrology (99%) compared with surgery (38.9%). TI was 2.3 (medical 2.5; surgical 1.5) and the UR was 96.2% (medical 99%; surgical 79.8%).

CONCLUSION: Blood utilization indicators align with international standards. Nephrology demonstrated high efficiency, whereas surgical practice showed a tendency towards precautionary crossmatching. Continuous monitoring of utilization indices and implementation of ordering policies such as MSBOS may further optimize utilization.

Keywords: blood utilization indicators, crossmatch-to-transfusion ratio, transfusion probability, transfusion index, utilization rate

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PP 032

ZNAČAJ RAZMJENE KRVI I KRVNIH KOMPONENTI U JEDINSTVENOM SISTEMU ZAVODA ZA TRANSFUZIJSKU MEDICINU REPUBLIKE SRPSKE – ISKUSTVA SLUŽBE ZA TRANSFUZIJSKU MEDICINU PRIJEDOR

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Uvod: Zavod za transfuzijsku medicinu Republike Srpske predstavlja jedinstven model organizacije transfuzijske medicine u regionu, zasnovan na centralizovanom upravljanju zalihama krvi i krvnih komponenti kroz četiri regionalna centra i pripadajućih šest službi za transfuzijsku medicinu.
Cilj: Prikazati značaj razmjene krvi i krvnih komponenti između Službe za transfuzijsku medicinu Prijedor i drugih centara i službi Zavoda za transfuzijsku medicinu Republike Srpske tokom desetogodišnjeg perioda.
Materijal i metode: Retrospektivno su analizirani podaci o razmjeni krvi i krvnih komponenti iz Službe za transfuzijsku medicinu Prijedor prema drugim centrima i službama Zavoda u periodu od 01.01.2016. do 01.01.2026. godine. Podaci su preuzeti iz informacionog sistema Zavoda. Analiziran je broj distribuisanih doza deplazmatisanih eritrocita i svježe smrznute plazme.
Rezultati: U posmatranom periodu iz Službe za transfuzijsku medicinu Prijedor distribuisano je ukupno 10.067 doza deplazmatisanih eritrocita. Najveći broj doza upućen je centru Banja Luka – 9.759 (96,9%), dok je prema ostalim centrima i službama distribuisano 308 (3,1%) doza. Istovremeno je distribuisana ukupno 9.071 doza svježe smrznute plazme. Najveći broj jedinica upućen je službama Foča – 3.605 (39,7%) i Kasindo – 3.044 (33,6%), što zajedno čini 73,3% ukupno poslane plazme. Prema centru Banja Luka distribuisano je 2.172 (23,9%) doze, dok je prema ostalim službama distribuisano 250 (2,8%) doza.
Zaključak: Jedinstvena organizacija Zavoda, omogućava racionalno korišćenje raspoloživih doza sigurne krvi, smanjenje mogućnosti isteka roka upotrebe i propadanja krvnih komponenti, te pravovremeno liječenje pacijenata na području cijele Republike Srpske.
Ključne riječi: transfuzijska medicina, razmjena krvi, krvne komponente

PP 032

THE IMPORTANCE OF BLOOD COMPONENTS EXCHANGE IN THE UNIQUE SYSTEM OF THE INSTITUTE FOR TRANSFUSION MEDICINE OF THE REPUBLIC OF SRPSKA - EXPERIENCES OF THE SERVICE FOR TRANSFUSION MEDICINE PRIJEDOR

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Introduction: The Institute for Transfusion Medicine of the Republic of Srpska represents a unique model of the organization of transfusion medicine in the region, based on the centralized management of blood component supplies through four regional centers and six related services for transfusion medicine.
Objective: To show the importance of the exchange of blood and blood components between the Service for Transfusion Medicine Prijedor and other centers and services of the Institute for Transfusion Medicine of the Republic of Srpska during a ten-year period.
Material and methods: Data on the exchange of blood components from the Service for Transfusion Medicine Prijedor to other centers and services of the Institute in the period from 01.01.2016 until 01.01.2026. were analyzed retrospectively. The data were taken from the Institute's information system. The number of distributed erythrocytes and fresh frozen plasma was analyzed.
Results: In the observed period, a total of 10,067 erythrocytes were distributed from the Service for Transfusion Medicine Prijedor. The largest number of doses was sent to the Banja Luka center - 9,759 (96.9%), while 308 (3.1%) doses were distributed to other centers and services. At the same time, a total of 9,071 doses of fresh frozen plasma were distributed. The largest number of units were sent to the services of Foča - 3,605 (39.7%) and Kasindo - 3,044 (33.6%), which make up 73.3% of the total plasma sent. 2,172 (23.9%) doses were distributed to the Banja Luka center, while 250 (2.8%) doses were distributed to other services.
Conclusion: The unique organization of the Institute enables the rational use of available doses of safe blood, the reduction of the possibility of the expiry date and deterioration of blood components, and the timely treatment of patients throughout the Republic of Srpska.
Key words: transfusion medicine, blood exchange, blood components

PP 033

TRANSFUZIJSKA MEDICINA IZMEĐU JAVNOG I PRIVATNOG ZDRAVSTVENOG SEKTORA – IZAZOVI, ODRŽIVOST I STRATEŠKI ZNAČAJ ZA ZDRAVSTVENI SISTEM

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Savremeni zdravstveni sistemi prolaze kroz značajne organizacione promjene obilježene rastom privatnog zdravstvenog sektora i postepenim prelaskom dijela zdravstvenih usluga iz javnog u privatni domen. Ovakve promjene neminovno utiču i na transfuzijsku medicinu, koja predstavlja jedan od najosjetljivijih i strateški najvažnijih segmenata svakog zdravstvenog sistema. Transfuzijska služba počiva na principima nacionalne koordinacije, samoodrživosti, bezbjednosti i kontinuirane dostupnosti krvi i krvnih komponenti, zbog čega zahtijeva poseban pristup u uslovima razvoja javno-privatnog modela zdravstvene zaštite.
Cilj rada je da ukaže na izazove sa kojima se transfuzijska medicina suočava u procesu širenja privatnog zdravstvenog sektora, te da istakne značaj transfuzijske službe u strategiji razvoja zdravstva jedne države. Poseban akcenat stavljen je na pitanja racionalne upotrebe krvi, standardizacije transfuzijskih procedura, digitalne povezanosti zdravstvenih ustanova, edukacije medicinskog kadra i razvoja modela javno-privatnog partnerstva u oblasti transfuzije.
Analiza dosadašnjih iskustava ukazuje da povećano učešće privatnih zdravstvenih ustanova dovodi do novih organizacionih i logističkih izazova u planiranju i distribuciji hemoprodukata, no istovremeno otvara mogućnost za unaprjeđenje kvaliteta, efikasnosti i primjene savremenih principa *Patient Blood Management*. U uslovima ograničenih resursa a rastućih potreba za krvnim komponentama, transfuzijska medicina postaje važan pokazatelj stabilnosti i otpornosti zdravstvenog sistema.
Rad naglašava da transfuzijska služba ne smije biti posmatrana isključivo kao prateća dijagnostičko-terapijska djelatnost, već kao ključni strateški resurs nacionalne zdravstvene bezbjednosti, uz integrisani pristup u kojem će transfuzijska medicina imati centralnu ulogu u planiranju kriznih kapaciteta, očuvanju samodovoljnosti u snabdijevanju krvlju i uspostavljanju održivog i bezbjednog modela zdravstvene zaštite u javnom i privatnom sektoru.
Ključne riječi: transfuzijska medicina, kvalitet u transfuziji, privatni zdravstveni sektor, *Patient Blood Management*, racionalna upotreba krvi

PP 033

TRANSFUSION MEDICINE BETWEEN PUBLIC AND PRIVATE HEALTH SECTOR - CHALLENGES, SUSTAINABILITY AND STRATEGIC SIGNIFICANCE FOR THE HEALTH SYSTEM

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Contemporary health systems are undergoing significant organizational changes marked by the growth of the private health sector and the gradual transition of part of health services from public to private domain. Such changes inevitably affect transfusion medicine, which represents one of the most sensitive and strategically important segments of any healthcare system. The transfusion service is based on the principles of national coordination, self-sustainability, safety and continuous availability of blood and blood components, which is why it requires a special approach in the conditions of the development of the public-private model of health care.
The aim is to point out the challenges that transfusion medicine faces in the process of expansion of private health sector, and to highlight the importance of the transfusion service in the health development strategy of a country. Special emphasis was placed on the issues of rational use of blood, standardization of transfusion procedures, digital connectivity of health institutions, education of medical staff and development of a public-private partnership model in the field of transfusion.
The analysis of past experiences indicates that the increased participation of private health institutions leads to new organizational and logistical challenges in the planning and distribution of haemoproducts, but at the same time it opens up the possibility of improving the quality, efficiency and application of modern principles of *Patient Blood Management*. In conditions of limited resources and growing needs for blood components, transfusion medicine becomes an important indicator of the stability and resilience of the health system.
We emphasize that the transfusion service must not be viewed exclusively as an accompanying diagnostic and therapeutic activity, but as a key strategic resource of national health safety, with an integrated approach in which transfusion medicine will play a central role in planning crisis capacities, preserving self-sufficiency in blood supply and establishing a sustainable and safe model of health care in the public and private sector.
Key words: transfusion medicine, quality in transfusion, private health sector, *Patient Blood Management*, rational use of blood

PP 034

QUALITY CONTROL – IDENTIFICATION OF SYSTEMIC NON-CONFORMITIES

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Introduction: The Quality Management System (QMS) in transfusion services includes structures, procedures, and resources to ensure the safety and efficiency of blood components. The quality control laboratory for final products is a key part of the QMS, enabling objective assessment of compliance with regulatory and international standards.
Aim: To present experience in establishing a quality control laboratory and to analyze quality control results of blood components according to EDQM Guide standards, with identification of non-conformities across the transfusion chain.
Methods: During a 17-month period, 571 blood components (red blood cells, platelets, plasma, cryoprecipitate) were tested. Sampling covered at least 1% of processed units in line with EDQM recommendations.
Results: Non-conformities were most frequent in red blood cell components, with about 20% showing reduced volume and hemoglobin concentration. Platelet components showed about 15% non-conformities, including lower platelet counts in buffy coat-derived concentrates and reduced counts in day 7 apheresis platelets. Additional issues were observed in collection, processing, storage conditions, and equipment availability, indicating systemic process deficiencies.
Conclusion: The quality control laboratory is essential for identifying critical points in the transfusion chain. Integration of results into the QMS enables corrective and preventive actions, continuous improvement, and improved safety of blood components in line with international standards.

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PP 035

HEALTHY INJURIES AT WORK WITH HEALTHCARE WORKERS

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INTRODUCTION Accidental injuries by health workers at work result in injury to a needle cut into a sharp object that is contaminated by blood or some other body fluid.
They pose a great risk of getting very serious infections, most commonly life-threatening.
PURPOSE OF THE WORK We showed the results of the observation of injuries with the sharp objects of health workers in the General hospital Bar in the period from 2014 to 2024 year. Reports are sent from each department separately as work-related injury to the Department of Hygiene and Epidemiology services. The report contains information on the identity of the injured person, the place, time and manner of the injury, or the type of bodily fluid to which exposure occurred.
RESULTS OF WORK The most common types of injury during the years of observation are stab wounds and needle sticks, followed by cuts from scalpels and glass. The rate of exposure to needle-stick infections is 0,69-3,11% and the risk of acquiring an infection is 0,006-0,03%, which aligns with European and global standards. Most stab injuries were recorded among mid-level medical staff.
CONCLUSION The protection of healthcare workers must be a priority. The use of safe medical equipment, medical waste disposal processes, continuous education, application of standardized health protection and treatment measures for contaminates individuals and promotion of the highest quality standards. It only takes one second for a needlestick incident to change a healthcare workers life forever. Measures taken within 72 hours of a puncture injury will reduce the risk of infection by 80%.
Key words: stab injuries, health workers, possibility of infection, protective measures

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PP 036

EPLET ANALIZA KAO DODATNI KRITERIJUM ZA IZBOR AFEREZNIH DAVALACA TROMBOCITA KOD PACIJENATA REFRAKTORNIH NA TRANSFUZIJE TROMBOCITA

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Uvod: Pri izboru davalaca trombocita, pored standardnih kriterijuma zasnovanih na HLA podudarnosti, rezultatima testa unakrsne reakcije i prisustvu donor-specifičnih antitela (DSA), eplet analiza predložena je kao dopunski pristup.
Cilj: Procena imunološkog značaja analize eplet nepodudarnosti u kontekstu prisustva DSA i rezultata testa unakrsne reakcije.
Materijal i metode: Retrospektivno je analizirano sedam pacijenata refraktornih na transfuzije trombocita. Za svakog pacijenta izabrano je šest do sedam davalaca trombocita. HLA tipizacija rađena je metodom PCR-SSO, anti-HLA antitela klase I detektovana su Luminex single-antigen bead metodom (SAB), a test unakrsne reakcije (crossmatch, CM) metodom komplement-zavisne citotoksičnosti (CDC). Ukupna eplet nepodudarnost i antitelima potvrđena eplet nepodudarnost procenjene su pomoću Mismatch Calculator alata u okviru Eplet Registry-ja. Davaoci su retrospektivno rangirani standardnim pristupom, eplet pristupom i kombinacijom ova dva pristupa.
Rezultati: Od ukupno 47 parova davalac–primalac, 14 je bilo DSA-negativno/CM-negativno, 29 DSA-pozitivno/CM-negativno, a četiri para DSA-pozitivna/CM-pozitivna. Nije bilo DSA-negativnih/CM-pozitivnih parova. Korelacija između standardnog i eplet rangiranja pokazala je promenljiv stepen slaganja (Spearmanov rho 0,071–0,771), bez statističke značajnosti. Najizraženiji doprinos eplet analize uočen je u DSA-pozitivno/CM-negativnoj grupi, u kojoj je izbor najbolje rangiranog davaoca promenjen kod 3 od 7 pacijenata (42%). Kombinovani algoritam nije menjao konačni izbor davaoca.
Zaključak: Eplet analiza može obezbediti dodatnu procenu imunološkog rizika, posebno kod DSA-pozitivnih/CM-negativnih parova, što podržava njenu primenu kao dopunskog alata u selekciji afereznih davalaca trombocita kod senzibilisanih pacijenata. Potrebna su istraživanja na većem broju pacijenata da bi se ovi nalazi potvrdili.
Ključne reči: trombocitna refraktarnost; aferezni davaoci trombocita; donor-specifična antitela; eplet analiza; unakrsna reakcija

PP 036

EPLET ANALYSIS AS AN ADDITIONAL TOOL FOR PLATELET DONOR SELECTION IN PATIENTS WITH PLATELET TRANSFUSION REFRACTORINESS

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Background: In addition to HLA matching, crossmatch results, and donor-specific antibodies (DSA), eplet analysis has been proposed as a complementary approach for platelet donor selection.
Objective: To evaluate the immunological significance of eplet mismatch analysis in the context of DSA and crossmatch results.
Materials and Methods: Seven patients with platelet transfusion refractoriness were retrospectively analyzed. Six to seven platelet donors were selected for each patient. HLA typing was performed using the PCR-SSO method, anti-HLA class I antibodies were detected using the Luminex single-antigen bead assay, and crossmatch (CM) testing was performed by complement-dependent cytotoxicity. Total and antibody-verified eplet mismatches were assessed using the Mismatch Calculator within the Eplet Registry. Donors were retrospectively ranked using the standard approach, the eplet-based approach, and a combination of both.
Results: Among 47 donor–recipient pairs, 14 were DSA-negative/CM-negative, 29 DSA-positive/CM-negative, and 4 DSA-positive/CM-positive. No DSA-negative/CM-positive pairs were observed. Correlation between standard and eplet-based donor rankings showed variable agreement (Spearman's rho 0.071–0.771) without statistical significance. The greatest impact of eplet analysis was observed in the DSA-positive/CM-negative group, where the highest-ranked donor changed in 3 of 7 patients (42%). The combined algorithm did not alter the final donor selection.
Conclusions: Eplet analysis may provide additional assessment of immunological risk, particularly in DSA-positive/CM-negative pairs, supporting its use as a complementary tool for platelet donor selection in sensitized patients. Larger studies are needed to confirm these findings.
Keywords: platelet transfusion refractoriness; platelet donors; donor-specific antibodies; eplet analysis; crossmatch

PP 037

PODUDARNOST HLA-B LIDER GENOTIPOVA I IMUNOGENETSKI RIZIK KOD PACIJENATA NAKON ALOGENE TRANSPLANTACIJE MATIČNIH ĆELIJA HEMATOPOEZE

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Uvod: HLA-B liderski genotipovi, određeni prisustvom aminokiseline na poziciji −21 (metionin ili treonin), utiču na aktivnost NK ćelija i modulaciju imunološkog odgovora. Njihovo razumevanje je značajno za selekciju donora i procenu imunogenetskog rizika kod pacijenata alogenu transplantaciju matičnih ćelija hematopoeze (MĆH).
Cilj: Ispitati učestalost HLA-B liderskih genotipova i njihov potencijalni uticaj na posttransplantacione komplikacije kod pacijenata nakon alogene transplantacije MĆH.
Metod: Analizirano je 22 pacijenta sa malignim hematološkim oboljenjima, lečenih u periodu 2015–2023. Svi su transplantirani od nesrodnih davalaca sa nepodudarnošću u HLA-B lokusu. Tipizacija je sprovedena PCR metodama, a genotipovi definisani BLEAT kalkulatorom.
Rezultati: Podudarnost HLA-B liderskih genotipova registrovana je kod 19 pacijenata (86,4%), dok je HLA-B liderska nepodudarnost utvrđena kod 3 pacijenta (13,6%). Kod sva tri pacijenta sa HLA-B liderskom nepodudarnošću dokazan je genotip TT. Analiza komplikacija pokazala je da je sepsa registrovana kod jednog pacijenta (4,5%) sa HLA-B liderskom nepodudarnošću, dok je relaps zabeležen kod dva pacijenta (9,1%). Akutna i hronična forma bolesti kalem protiv domaćina nije zabeležena. Kod pacijenata sa HLA B lidreskom podudarnošću, relaps je registrovan kod 4 (18,2%), sepsa kod 5 (22,7%), dok su akutni (aGvHD) i hronični (hGvHD) oblik bolesti kalem protiv domaćina zabeležen kod po 8 pacijenata (36,4%). Slaba funkcija grafta registrovana je kod 2 pacijenta (9,1%).
Zaključak: Zbog ograničenog broja pacijenata sa nepodudarnošću, nalazi imaju preliminarni karakter. Dominacija TT genotipa i registrovane komplikacije ukazuju na potrebu za daljim istraživanjima u okviru većih multicentričnih studija radi optimizacije transplantacione prakse.
Ključne reči:HLA-B lider, učestalost genotipova, transplantacija matičnih ćelija, NK ćelije, selekcija donora, imunogenetika

PP 037

MATCHING OF HLA-B LEADER GENOTYPES AND IMMUNOGENETIC RISK IN PATIENTS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: HLA-B leader genotypes, defined by the presence of methionine or threonine at position −21, influence natural killer (NK) cell activity and modulation of immune responses. Understanding their role is important for donor selection and assessment of immunogenetic risk in patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT).
Aim: To investigate the distribution of HLA-B leader genotypes and their potential impact on post-transplant complications in patients following allogeneic HSCT.
Methods: A cohort of 22 patients with malignant hematological disorders treated between 2015 and 2023 was analyzed. All patients received transplants from unrelated donors with HLA-B locus mismatch. Genotyping was performed using PCR-based methods, and leader genotypes were defined with the BLEAT calculator.
Results: HLA-B leader match was observed in 19 patients (86.4%), whereas mismatch was identified in 3 patients (13.6%). In the mismatch group, all patients have the TT genotype. In the mismatch group, sepsis occurred in one patient (4.5%) and relapse in two patients (9.1%), with no cases of acute or chronic graft-versus-host disease (GvHD). Among patients with match HLA-B leader genotypes, relapse was observed in four (18.2%), sepsis in five (22.7%), and both acute and chronic GvHD in eight patients each (36.4%). Poor graft function was documented in two patients (9.1%).
Conclusion: Due to the limited number of patients with HLA-B leader mismatch, these findings should be considered preliminary. The predominance of the TT genotype and the associated complications need to be investigated in larger multicenter studies to optimize transplantation practice.
Keywords: HLA-B leader, genotype frequency, hematopoietic stem cell transplantation, NK cells, donor selection, immunogenetics

PP 038

ANTIOKSIDATIVNI EFEKTI MELATONINA U TKIVU TESTISA TOKOM ENDOTOKSEMIJE IZAZVANE LIPOPOLISAHARIDOM ESCHERICHIA COLI

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Uvod: Sepsa predstavlja životno ugrožavajući sindrom uzrokovan poremećenim imunskim odgovorom domaćina na infekciju, koji dovodi do disfunkcije organa. Lipopolisaharid (LPS), glavna komponenta spoljašnje membrane gram-negativnih bakterija, aktivacijom TLR4/NF-κB signalnog puta indukuje oslobađanje proinflamatornih citokina i pojačanu produkciju reaktivnih kiseoničnih vrsta, što rezultira oksidativnim stresom i oštećenjem tkiva. Melatonin je endogeni indolamin sa izraženim antioksidativnim i imunomodulatornim svojstvima, koji direktno uklanja slobodne radikale i stimuliše aktivnost antioksidativnih enzima.
Cilj: Cilj istraživanja bio je da se proceni antioksidativni efekat melatonina u tkivu testisa pacova sa endotoksemijom izazvanom lipopolisaharidom Escherichia coli, analizom aktivnosti katalaze (CAT), ksantin-oksidaze (XO), glutation-reduktaze (GR) i glutation-S-transferaze (GST).
Materijal i metode: Dvadeset osam mužjaka Wistar albino pacova podeljeno je u četiri grupe (n=7): Kontrola, Mel, LPS i LPS+Mel. Melatonin (50 mg/kg TT) primenjen je oralno, dok je LPS (Escherichia coli O111; 10 mg/kg TT) aplikovan intraperitonealno. Dvadeset sati nakon tretmana životinje su žrtvovane u dubokoj anesteziji, nakon čega je izolovano tkivo testisa i pripremljen 10% homogenat za određivanje aktivnosti antioksidativnih enzima.
Rezultati: Endotoksemija je izazvala značajno smanjenje aktivnosti CAT ($p<0,05$) i GST ($p<0,001$), uz povećanje aktivnosti XO ($p<0,001$) i GR ($p<0,001$) u odnosu na kontrolu. Primena melatonina značajno je smanjila aktivnost XO ($p<0,01$) i GR ($p<0,05$), dok je povećala aktivnost GST ($p<0,001$) u odnosu na LPS grupu, ukazujući na ublažavanje oksidativnog oštećenja testisa.
Zaključak: Melatonin je pokazao značajan antioksidativni i citoprotektivni potencijal u eksperimentalnoj endotoksemiji, normalizujući aktivnost ključnih enzima antioksidativne zaštite u tkivu testisa. Dobijeni rezultati ukazuju da melatonin predstavlja perspektivnu pomoćnu terapijsku strategiju za ublažavanje oksidativnog oštećenja reproduktivnog sistema tokom sepse, što zahteva potvrdu u daljim preklinčkim i kliničkim istraživanjima.

Ključne reči: melatonin; endotoksemija; lipopolisaharid; oksidativni stres; testis

PP 038

ANTIOXIDANT EFFECTS OF MELATONIN IN TESTICULAR TISSUE DURING ENDOTOXEMIA INDUCED BY ESCHERICHIA COLI LIPOPOLYSACCHARIDE

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Introduction: Sepsis is a life-threatening syndrome caused by a dysregulated host response to infection, leading to organ dysfunction. Lipopolysaccharide (LPS), the major component of the outer membrane of Gram-negative bacteria, activates the TLR4/NF-κB signaling pathway, inducing the release of pro-inflammatory cytokines and excessive production of reactive oxygen species, ultimately resulting in oxidative stress and tissue injury. Melatonin is an endogenous indolamine with potent antioxidant and immunomodulatory properties that directly scavenges free radicals and enhances the activity of endogenous antioxidant enzymes.
Aim: This study aimed to evaluate the antioxidant effects of melatonin in the testicular tissue of rats with Escherichia coli lipopolysaccharide-induced endotoxemia by analyzing the activities of catalase (CAT), xanthine oxidase (XO), glutathione reductase (GR), and glutathione S-transferase (GST).
Materials and Methods: Twenty-eight male Wistar albino rats were randomly assigned to four groups (n=7): Control, Mel, LPS, and LPS+Mel. Melatonin (50 mg/kg body weight) was administered orally, whereas LPS (Escherichia coli O111, 10 mg/kg body weight) was administered intraperitoneally. Twenty hours after treatment, the animals were euthanized under deep anesthesia. Testicular tissue was collected, and a 10% tissue homogenate was prepared for the determination of antioxidant enzyme activities.
Results: Endotoxemia significantly decreased CAT ($p<0.05$) and GST ($p<0.001$) activities while increasing XO ($p<0.001$) and GR ($p<0.001$) activities compared with the control group. Melatonin administration significantly reduced XO ($p<0.01$) and GR ($p<0.05$) activities and increased GST activity ($p<0.001$) compared with the LPS group, indicating attenuation of oxidative damage in testicular tissue.
Conclusion: Melatonin exhibited significant antioxidant and cytoprotective effects in experimental endotoxemia by modulating the activity of key antioxidant enzymes in testicular tissue. These findings suggest that melatonin may represent a promising adjunctive therapeutic strategy for reducing sepsis-induced oxidative damage to the male reproductive system, although further preclinical and clinical studies are warranted.

Keywords: melatonin; endotoxemia; lipopolysaccharide; oxidative stress; testis.

PP 039

TRIAL IN MILITARY MEDICAL ACADEMY USING THE NEW ANTI – DARATUMUMAB REAGENT

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Objective: To show our experience with the new anti – idiotypic anti – daratumumab monoclonal antibody from BioRad.
Materials and methods: Standart immunohematology antibody screening has been performed using column agglutionation technology with LISS/Coombs cards and ID – DiaCell I-II-III cells and DiaClon Complete Crossmatch cards for compatibility test.
Results: Eleven patients were included in this trial. Before starting the therapy with Daratumumab each of the patients underwent a standart immunohematology antibody screening was negative. They were tested again during different stages of their treatment. IAGT became positive showing pan reaction.
As first step all the patients samples were prepared according 10% protocol /10µl of anti-idiotypic anti-daratumumab and 100µl plasma/. Then standart IAGT was performed. Nine of the samples were efficiently neutralized. Two samples remained positive. We used these 10% plasma for identicifation using ID – DiaPanel with 11 test cells and it showed pan reactivity with all cells. The next step was these patients samples to be prepared according 20% protocol /20µl of anti-idiotypic anti-daratumumab and 100µl plasma/ followed by standart IAGT test which was negative.
Before the neutralization each patient sample was used for standart compatibility test using DiaClon Complete Crossmatch cards. The result showed no compatibility because of positive IAGT. After the neutralization /10% or 20% protocol/ the samples were used for compatibility tests. IAGT was negative.
Conclusion: Despite the small number of patients has a great impact on pretransfusion testing and transfusion safety of patients undergoing treatment with Daratumumab.
Keywords: daratumumab, anti – idiotypic, monoclonal antibody, pretransfusion testing

PP 039

PP 040

RANE KOMPLIKACIJE KAO FAKTORI PRIHVATANJA KALEMA I RAZVOJA ENDOTELIJALNOG OŠTEĆENJA NAKON ALOGENE TRANSPLANTACIJE MATIČNIH ĆELIJA HEMATOPOEZE-PILOT STUDIJA

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Uvod: Rani ishodi nakon alogene transplantacije matičnih ćelija hematopoeze determinisani su složenim interakcijama između infektivnih, imunoloških i vaskularnih komplikacija. Razumevanje međusobne povezanosti ovih događaja je od ključnog značaja za predviđanje hematološkog oporavka i ranog morbiditeta.
Cilj: Analizirati uticaj ranih posttransplantacionih komplikacija na kinetiku prihvatanja kalema i pojavu endotelijalnog sindroma.
Materijal i metode: Retrospektivna studija obuhvatila je 43 bolesnika lečenih na Klinici za hematologiju UKCS u periodu 2017–2019. Podaci su prikupljeni iz *Follow-up* Registra davalaca MĆH Srbije i istorija bolesti. Kinetika engraftmenta procenjivana je analizom kumulativne incidencije, pri čemu je smrt pre engraftmenta posmatrana kao kompetitivni događaj. Zbog ograničenog broja ispitanika, povezanost ranih komplikacija i kinetike engraftmenta analizirana je prvenstveno primenom neparametrijskih testova, uključujući Mann–Whitney U test. Statistička analiza sprovedena je korišćenjem programskog jezika R.
Rezultati: Utvrđena je značajna povezanost između infektivnih komplikacija i poremećene funkcije kalema. CMV reaktivacija bila je povezana sa pojavom slabosti kalema (p=0,02) i produženom zavisnošću od transfuzija trombocita (p=0,032). Značajna povezanost između aGvHD i razvoja endotelijalnih sindroma VOD/TMA (p=0,011) dodatno potvrđuje pretpostavljene zajedničke imunološko-endotelijalne mehanizme njihovog nastanka. Hemoragični cistitis korelirao je sa odloženim engraftmentom neutrofila (p=0,008) i trombocita (p=0,03), kao i sa slabijom funkcijom kalema (p=0,005).
Zaključak: Ova pilot analiza ukazuje da rane posttransplantacione komplikacije nisu izolovani događaji, već predstavljaju međusobno povezane procese koji značajno utiču na hematološki oporavak. Zbog ograničene veličine uzorka, dobijeni rezultati zahtevaju potvrdu u većoj, multicentričnoj kohorti.

Ključne reči: alogena transplantacija matičnih ćelija hematopoeze, CMV reaktivacija, akutna bolest kalema protiv domaćina, endotelijalni sindromi, funkcija kalema

PP 040

EARLY POST-TRANSPLANT COMPLICATIONS AS DETERMINANTS OF GRAFT ENGRAFTMENT AND ENDOTHELIAL INJURY FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A PILOT STUDY

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Introduction: Early outcomes following allogeneic hematopoietic stem cell transplantation (allo-HSCT) are determined by complex interactions among the donor's, patient's, and transplant- related factors, as well as infectious, immunological, and endothelial complications.
Objective: To evaluate the association between early post-transplant complications with engraftment kinetics and the development of endothelial syndromes following allo-HSCT.
Methods: This retrospective study included 43 patients treated at the Clinic for Hematology, University Clinical Center of Serbia, between 2018 and 2019. Data were collected from the Follow-up of the Serbian BMDR and medical records. Due to the limited sample size, engraftment kinetics were assessed by cumulative incidence analysis. Correlation between early complications and engraftment kinetics was primarily assessed using non-parametric tests, including Mann–Whitney U test. Statistical analysis was performed using R software.
Results: A significant correlation was observed between infectious complications and impaired graft function. CMV reactivation was associated with poor graft function (p = 0.02) and prolonged platelet transfusion dependence (p = 0.032). A significant association between aGvHD and the development of endothelial syndromes VOD/TMA (p=0.011) supports the concept of shared pathophysiological pathways and overlapping mechanisms of endothelial damage. Hemorrhagic cystitis emerged as a marker of increased systemic burden, correlating with delayed neutrophil (p=0.008) and platelet engraftment (p=0.03), as well as poorer graft function (p=0.005).
Conclusion: This pilot analysis suggests that early post-transplant complications represent interconnected processes within an infectious–immunological–endothelial axis influencing graft recovery. Given the limited sample size, these findings should be interpreted as hypothesis-generating and require validation in a larger, preferably multicenter cohort.

Keywords:
allogeneic hematopoietic stem cell transplantation, engraftment, CMV reactivation, acute graft-versus-host disease, endothelial syndromes, graft function

PP 041

KOMPARATIVNA EVALUACIJA DEFORMABILNOSTI ERITROCITA PROTOČNOM CITOMETRIJOM I EKTACITOMETRIJOM: MOGUĆ PUT KA UNAPREĐENJU TRANSFUZIJSKE PRAKSE

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Uvod: Deformabilnost eritrocita predstavlja ključni parametar mikrocirkulatornog protoka i isporuke kiseonika, ali je njeno ispitivanje zanemareno u transfuzijskoj praksi. Deformabilnost eritrocita se smanjuje tokom skladištenja usled akumulacije oštećenja, a dodatno je modulirana donor-specifičnim faktorima (uzrast, pol, način života, itd.). Iako se ektacitometrija smatra referentnom metodom za procenu deformabilnosti eritrocita, njena primena u rutinskoj praksi je ograničena [1]. Protočna citometrija bez primene obeleživača predstavlja metodu sa potencijalom za procenu mehaničkih osobina eritrocita, zbog efikasnosti u merenju velikog broja pojedinačnih ćelija i široke dostupnosti u kiničko-bolničkim centrima [2].
Cilj: U ovoj studiji ispitana je povezanost između parametara deformabilnosti dobijenih protočnom citometrijom bez primene oveleživača i konvencionalnom ektacitometrijom u uzorcima sveže pune krvi zdravih dobrovoljaca, radi procene potencijala protočne citometrije kao komplementarne metode za procenu deformabilnosti.
Materijal i metode: U studiju je uključeno 20 svežih uzoraka pune krvi zdravih dobrovoljaca (starosti 35–57 godina; 14 muškaraca, 6 žena). Eritrociti su izolovani i analizirani pomoću ektacitometra RheoScan D-300 (RheoMeditech Inc., Koreja) i BD FACSCalibur protočnog citometra (Becton Dickinson, SAD), prema protokolima optimizovanim i razvijenim u našoj prethodnoj studiji [3].
Rezultati: Suprotno standardnim merenjima deformabilnosti, protočna citometrija je omogućila detekciju interindividualnih razlika u oksidativnom statusu zdravih donora. Prisustvo fluorescentnih pikova različitih površina, poreklom od oksidovanih eritrocita, ukazuje da oksidacija indukuje pojavu subpopulacija eritrocita sa povećanim intenzitetom autofluorescencije i povećanom agregabilnošću.
Zaključak: S obzirom na to da mehanička svojstva eritrocita mogu značajno uticati na posttransfuzionu efikasnost, procena deformabilnosti protočnom citometrijom na nivou pojedinačnih ćelija predstavlja obećavajuću, brzu i široko dostupnu alternativu ili dopunu standardnoj ektacitometriji.

Ključne reči: crvena krvna zrnca, deformabilnost, hemoreologija, mehanobiologija

PP 041

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Ključne reči: crvena krvna zrnca, deformabilnost, hemoreologija, mehanobiologija

PP 042

PERSISTENT HEAVY MENSTRUAL BLEEDING AFTER MENARCHE AS THE INITIAL PRESENTATION OF PLATELET DYSFUNCTION: A CASE REPORT

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Background: Heavy menstrual bleeding (HMB) at menarche is a critical clinical warning sign of an underlying inherited or acquired bleeding disorder. Although anovulatory cycles account for the majority of abnormal uterine bleeding cases in adolescents, platelet function disorders must be considered when bleeding is severe, prolonged, or refractory to initial management, even in the presence of normal routine coagulation studies.

Case Presentation: A 13-year-old, previously healthy adolescent girl presented with persistent HMB that initiated immediately at menarche (at age 12) and sustained for approximately 10 months. Prior to presentation, she had not received hormonal therapy but was maintained on continuous oral iron supplementation. Complete blood count (CBC) revealed microcytic anemia with a completely normal platelet count. Initial routine hemostatic screening, prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time was performed at the Center for Transfusion Medicine – Shtip and the results are in normal range. Due to the clinical presentation, von Willebrand disease was initially suspected as the primary differential diagnosis. Consequently, the patient was referred to Hemophilia Center at the National Institute for Transfusion Medicine in Skopje for advanced hematological workup. Comprehensive coagulation and screening assays—including factor VIII activity, von Willebrand factor (vWF) antigen and activity, antithrombin III, protein C, protein S, lupus anticoagulant, and D-dimer—were all within physiological limits, effectively ruling out von Willebrand disease. However, specialized platelet aggregation testing revealed significantly impaired responses to adenosine diphosphate (ADP) (51%), collagen (54%), and ristocetin (66%), establishing a diagnosis of a platelet function disorder (Thrombocytopathy). The patient was advised to strictly avoid antiplatelet medications and was successfully managed with oral iron supplementation combined with targeted tranexamic acid therapy during menorrhagia episodes (10-15mg/kg BW per day, divided into three daily doses for 3-5 days).

Conclusion: Persistent HMB from the onset of menarche warrants a comprehensive evaluation for underlying bleeding disorders, even when routine coagulation profiles and platelet counts appear reassuring. This case underscores the diagnostic necessity of specialized platelet function testing, particularly when highly suspected conditions like von Willebrand disease are excluded, in adolescents with unexplained, prolonged menstrual bleeding. Early recognition of thrombocytopathy is pivotal to mitigating future hemorrhagic risks during surgical interventions, trauma, and reproductive life.

PP 042

PP 043

PROCJENA PODUDARNOSTI IZMEĐU KAPILARNOG POCT I STANDARDNOG LABORATORIJSKOG MJERENJA INR KOD PACIJENATA NA VKA TERAPIJI

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Uvod: Point-of-care testiranje (POCT) omogućava brzo određivanje INR iz kapilarne krvi, što može unaprijediti monitoring pacijenata na oralnoj antikoagulantnoj terapiji antagonistima vitamina K (VKA). Klinička primjena POCT uređaja zahtijeva odgovarajuće slaganje sa laboratorijskim metodama.

Cilj: Procijeniti slaganje kapilarnog POCT određivanja INR na uređaju COAG S (Diagon Ltd.) sa standardnim laboratorijskim određivanjem INR na ACL ELITE Pro analizatoru kod pacijenata na VKA terapiji.

Materijal i metode: U prospektivnu studiju uključena su 72 pacijenta na VKA terapiji. Kapilarni i venski uzorci uzimani su simultano za POCT i laboratorijsko određivanje INR. Slaganje između metoda procijenjeno je Bland–Altman analizom, uz korelacijsku i inferencijalnu statistiku. Klinički prihvatljiva razlika definisana je kao ≤0,5 INR jedinica. Provedena je podgrupna analiza prema INR opsezima (<2, 2–3 i >3).

Rezultati: Studija je obuhvatila 45 muškaraca i 27 žena, srednje dobi 63,6±11,0 godina. Srednja vrijednost kapilarnog INR iznosila je 2,41±0,86, dok je srednja laboratorijska vrijednost INR iznosila 2,65±0,93. Utvrđena je umjerena povezanost metoda (r=0,605; p<0,001). Bland–Altman analiza pokazala je bias od –0,24 uz 95% granice slaganja od –1,80 do +1,33. Klinički prihvatljivu razliku (≤0,5 INR) imalo je 50,0% pacijenata. Podgrupna analiza pokazala je progresivno širenje granica slaganja pri višim INR vrijednostima: INR <2 (LoA: –1,15 do +0,85), INR 2–3 (LoA: –1,73 do +1,24) i INR >3 (LoA: –2,84 do +2,14).

Zaključak: Kapilarno POCT određivanje INR na uređaju COAG S pokazalo je nezadovoljavajuće slaganje sa standardnim laboratorijskim određivanjem INR, posebno pri višim INR vrijednostima. Dobijeni rezultati ukazuju da COAG S zahtijeva dodatnu validaciju prije rutinske primjene.

Ključne riječi: INR, point-of-care testiranje, Bland–Altman analiza, antagonisti vitamina K, usporedba metoda

PP 043

ASSESSMENT OF AGREEMENT BETWEEN CAPILLARY POCT AND STANDARD LABORATORY INR MEASUREMENT IN PATIENTS ON VKA THERAPY

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Introduction: Point-of-care testing (POCT) enables rapid INR determination from capillary blood, potentially improving monitoring of patients on oral anticoagulant therapy with vitamin K antagonists (VKA). Clinical application of POCT devices requires adequate agreement with laboratory methods.

Aim: To assess agreement between capillary POCT INR measurement using the COAG S device (Diagon Ltd.) and standard laboratory INR measurement on the ACL ELITE Pro analyser in patients on VKA therapy.

Materials and methods: This prospective study included 72 patients on VKA therapy. Capillary and venous samples were collected simultaneously for POCT and laboratory INR determination. Agreement between methods was assessed using Bland–Altman analysis and inferential statistics. Clinically acceptable difference was defined as ≤0.5 INR units. Subgroup analysis was performed according to INR ranges (<2, 2–3, and >3).

Results: The study included 45 men and 27 women, mean age 63.6±11.0 years. Mean capillary INR was 2.41±0.86, while mean laboratory INR was 2.65±0.93. Moderate correlation between methods was found (r=0.605; p<0.001). Bland–Altman analysis showed a bias of –0.24 with 95% limits of agreement of –1.80 to +1.33. Clinically acceptable difference (≤0.5 INR) was achieved in 50.0% of patients. Subgroup analysis showed progressive widening of agreement limits at higher INR values: INR <2 (LoA: –1.15 to +0.85), INR 2–3 (LoA: –1.73 to +1.24), and INR >3 (LoA: –2.84 to +2.14).

Conclusion: Capillary POCT INR measurement using the COAG S device demonstrated unsatisfactory agreement with standard laboratory INR measurement, particularly at higher INR values. COAG S requires additional validation before routine clinical use.

Keywords: INR, point-of-care testing, Bland–Altman analysis, vitamin K antagonists, method comparison

PP 044

PRIKAZ PODATAKA IZ NACIONALNOG REGISTRA UROĐENIH KOAGULOPATIJA

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Uvod. Nacionalni Registar urođenih koagulopatija se od osnivanja 1963. godine nalazi u Institutu za transfuziju krvi Srbije i predstavlja centralnu bazu podataka o pacijentima sa hemofiljom, von Willebrandovim oboljenjem i retkim koagulopatijama. **Cilj.** Prikazati aktuelne podatke o pacijentima i preparatima za lečenje. **Materijal i metode** Analizirali smo aktuelne podatake iz Nacionalnog Registra. **Rezultati:** U Srbiji je do decembra 2025. godine registrovano 1064 pacijenata sa urođenim koagulopatijama - 493 pacijenta sa hemofilijom A (HA) , 98 sa hemofilijom B (HB), 357 sa von Willebrand-ovim oboljenjem (VWB) i 116 sa retkim koagulopatijama (RK). Težak oblik HA je prisutan kod 195 (39,6%), umeren oblik kod 46 (9,3%) i blag oblik kod 252 (51,1%) pacijenata. Među 98 pacijenata sa HB 31 (31,6%) ima težak oblik, 16 (16,3%) je sa umerenim i 51 (52,1 %) sa blagim oblikom oboljenja. Inhibitori su prisutni kod 15 pacijenta sa HA. Od 357 (143 muškaraca i 214 žena) pacijenata sa VWB, 21 (5,9%) ima težak oblik, 96 (26,9%), umeren oblik i 240 (67,2%) blag oblik oboljenja. Od 114 pacijenata sa retkim koagulopatijama težak oblik ima 20 pacijenata - 2 pacijenta sa afibrinogenemijom, 2 sa kombinovanim deficitom FV+FVIII, 10 sa deficitom FVII i 6 sa deficitom FXIII. Lečenje pacijenata se sprovodi u 9 tercijarnih centara - na klinikama za hematologiju i pedijatriju u Beogradu, Novom Sadu, Nišu i Kragujevcu i 30 sekundarnih zdravstvenih centara. Svih 226 (100%) pacijenata sa teškim oblicima HA i HB nalaze se na redovnoj profilaksi, kao i 10/21 (47%) pacijenata sa teškim oblikom VWB. Pacijenti sa teškim oblicima retkih koagulopatija su na redovnoj profilaksi u skladu sa kliničkom procenom lekara. Potrošnja koncentrata FVIII u 2024. je dostigla 3,4 IJ/stanovniku, koncentrata, a FIX 1.10 IJ/stanovniku . Ovo je višestruko povećanje u odnosu na 2000-tu godinu (0,27 IJ/stanovniku za koncentrat FVIII i 0,03 IJ/stanovniku za koncentrat FIX). Od 2020. je registrovan emicizumab koji se primenjuje kod 85 pacijenata sa HA i 13 pacijenata sa HA sa inhibitorima.
Zaključak. Nacionalni registar urođenih koagulopatija predstavlja značajan insturment za planiranje i unapređenje zdravstvene zaštite pacijenata preko kontinuirane saradnje udruženja pacijenata sa hemofilijom, zdravstvenih i nadležnih državnih institucija.
Ključne reči: hemofilija, von Willebrand, retke, koagulopatije, registar

PP 044

OVERVIEW OF DATA FROM THE NATIONAL REGISTRY OF INHERITED COAGULATION DISORDERS

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Introduction. Since its establishment in 1963, the National Registry of Inherited Coagulation Disorders has been located at the National Blood Transfusion Institute of Serbia and represents the central database of patients with hemophilia, von Willebrand disease, and rare coagulation disorders.**Aim**. To present current data on patients and treatment products.**Material and Methods.** Current data from the National Registry were analyzed.**Results.** By December 2025, a total of 1,064 patients with inherited coagulation disorders had been registered in Serbia: 493 patients with hemophilia A (HA), 98 with hemophilia B (HB), 357 with von Willebrand disease (VWD), and 116 with rare bleeding disorders (RBDs). Severe HA was present in 195 (39.6%) patients, moderate HA in 46 (9.3%), and mild HA in 252 (51.1%) patients. Among 98 patients with HB, 31 (31.6%) had severe disease, 16 (16.3%) moderate disease, and 51 (52.1%) mild disease. Inhibitors were present in 15 patients with HA. Among 357 patients with VWD (143 males and 214 females), 21 (5.9%) had severe disease, 96 (26.9%) moderate disease, and 240 (67.2%) mild disease. Of 116 patients with rare coagulation disorders, 20 had severe forms: 2 with afibrinogenemia, 2 with combined FV+FVIII deficiency, 10 with FVII deficiency, and 6 with FXIII deficiency. Treatment is provided in 9 tertiary care centers, at hematology and pediatric clinics in Belgrade, Novi Sad, Nis, and Kragujevac, as well as in 30 secondary healthcare centers. All patients with severe HA and HB are on regular prophylaxis, as are 10/21 (47%) patients with severe VWD. Patients with severe forms of rare coagulation disorders receive regular prophylaxis according to the physician's clinical assessment. Consumption of FVIII concentrates in 2024 reached 3.4 IU per capita, while FIX concentrate consumption reached 1.10 IU per capita, representing a marked increase compared with the year 2000 (0.27 IU per capita for FVIII concentrate and 0.03 IU per capita for FIX concentrate). Since 2020, emicizumab has been registered and is currently used in 85 patients with HA and 13 patients with HA with inhibitors. **Conclusion.** The National Registry of Inherited Coagulation Disorders represents an important instrument for planning and improving healthcare for patients through continuous cooperation between hemophilia patients association, healthcare institutions and relevant governmental authorities.
Key words: haemophilia, von Willebrand, rare, bleeding, disorders, registry

PP 045

EKSTRAKORPORALNA IMUNOMODULACIJA I AFEREZNI PRISTUPI NAKON HSV-1 ENCEFALITISA

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Uvod: Savremena transfuziologija sve više uključuje terapijske afereze kao dio multidisciplinarnog pristupa liječenju imunološki posredovanih i neuroinflamatornih oboljenja. Nakon HSV-1 encefalitisa kod određenog broja pacijenata dolazi do razvoja prolongirane neuroinflamacije i perzistentnog neurokognitivnog deficita uprkos adekvatno sprovedenoj antivirusnoj terapiji.
Cilj rada: Prikazati klinički značaj terapijske membranske plazmafereze u modulaciji inflamatornog odgovora kod postinfektivnog neurološkog pogoršanja nakon HSV-1 encefalitisa.
Prikaz slučaja: Pacijent star 54 godine hospitalizovan je zbog potvrđenog HSV-1 encefalitisa sa kliničkom slikom febrilnosti, poremećaja svijesti i progresivnog neurokognitivnog oštećenja. Nakon sprovedene antivirusne terapije registrovana je negativizacija viroloških nalaza, uz perzistentne neurološke simptome, limfocitnu pleocitozu i znake kontinuirane inflamacije. U terapijski protokol uključene su četiri sesije membranske plazmafereze u kombinaciji sa dodatnim procedurama ekstrakorporalne modulacije krvi.
Rezultati: Tokom praćenja evidentirano je postepeno poboljšanje kognitivnih funkcija, govora i funkcionalnog statusa pacijenta. Klinički odgovor ukazuje na potencijalnu ulogu terapijske afereze u redukciji cirkulišućih inflamatornih medijatora i uspostavljanju imunološke homeostaze kod postvirusnih neuroinflamatornih stanja.
Zaključak: Membranska plazmafereza predstavlja perspektivnu adjuvantnu terapijsku opciju u okviru savremene transfuziološke prakse kod kompleksnih neuroimunoloških poremećaja. Dalja istraživanja biomarkera inflamacije i efekata terapijske afereze mogu doprinijeti razvoju personalizovanih protokola liječenja u neurotransfuziologiji.
Ključne riječi: terapijska afereza, HSV-1 encefalitis, neuroinflamacija, imunomodulacija, transfuziologija

PP 045

EXTRACORPOREAL IMMUNOMODULATION AND APHERESIS APPROACHES FOLLOWING HSV-1 ENCEPHALITIS

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Introduction: Modern transfusion medicine increasingly incorporates therapeutic apheresis into multidisciplinary management strategies for immune-mediated and neuroinflammatory disorders. Following HSV-1 encephalitis, a subset of patients may develop prolonged neuroinflammation and persistent neurocognitive impairment despite adequate antiviral therapy.

Objective: To present the clinical relevance of membrane plasmapheresis in modulation of inflammatory responses in post-infectious neurological deterioration after HSV-1 encephalitis.
Case Presentation: A 54-year-old patient was hospitalized with confirmed HSV-1 encephalitis manifested by fever, altered consciousness, and progressive neurocognitive dysfunction. Although antiviral therapy resulted in virological clearance, persistent neurological symptoms, lymphocytic pleocytosis, and ongoing inflammatory activity remained present. The therapeutic protocol included four sessions of membrane plasmapheresis combined with adjunct extracorporeal blood modulation procedures.
Results: Follow-up demonstrated gradual improvement in cognitive performance, speech function, and overall functional recovery. Clinical response suggests a potential role of therapeutic apheresis in reducing circulating inflammatory mediators and restoring immune homeostasis in post-viral neuroinflammatory conditions.
Conclusion: Membrane plasmapheresis represents a promising adjunctive therapeutic option within contemporary transfusion medicine practice for complex neuroimmunological disorders. Further investigations of inflammatory biomarkers and therapeutic apheresis outcomes may contribute to the development of personalized treatment protocols in neurotransfusion medicine.
Keywords: therapeutic apheresis, HSV-1 encephalitis, neuroinflammation, immunomodulation, transfusion medicine

PP 046

QUALITY CONTROL OF FRESH FROZEN PLASMA IN THE PERIOD 2022–2025 AT THE INSTITUTE FOR TRANSFUSION MEDICINE OF REPUBLIC OF NORTH MACEDONIA

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Introduction: Quality control of fresh frozen plasma (FFP) is mandatory and ensures biologically active, sterile, and safe FFP for clinical application and successful transfusion.
Aim: To analyze the results of the performed quality control of FFP in the Department for Quality Assurance and Quality Control at the Institute for Transfusion Medicine of Republic North Macedonia (RNM).
Materials and Methods: This is a retrospective analysis of data from protocols and reports maintained in the Department for Quality Assurance and Control at the Institute of Transfusion Medicine of RNM during the period 2022–2025.
Results: During the period 2022–2025, quality control was performed on a total of 314 units of FFP, of which 246 units after processing (before freezing) and 68 units after thawing.
In 2022, 58 units of FFP were controlled, with 95% meeting the quality criteria. Three units had lower factor VIII values than permitted (≥70 IU in 100 ml).
In 2023, 84 units of FFP were controlled, with 94% meeting the quality criteria. Three units had higher residual leukocyte values than permitted (<0.1 × 10^9/L per unit), and two units had lower factor VIII values than permitted.
In 2024, 35 units of FFP were controlled, with 91% meeting the quality criteria. One unit had higher residual leukocyte values than permitted, and two units had lower factor VIII values than permitted.
In 2025, 137 units of FFP were controlled, with 100% meeting the quality criteria.
Conclusion: Based on the obtained results of the quality control of FFP in the period 2022–2025, 95% of the units met the quality criteria, with a tendency toward improvement in the production process of FFP, thereby fulfilling healthcare standards.
Keywords: Quality control, Fresh frozen plasma, Healthcare standards

PP 046

8. KONGRES
TRANSFUZIOLOGA SRBIJE
AKREDITOVAN KAO MEĐUNARODNI
TREĆI MEĐUNARODNI
KONGRES U ORGANIZACIJI UTS

29-31. OKTOBAR, 2026.
SAVA CENTAR, BEOGRAD, SRBIJA



8TH TRANSFUSION
MEDICINE CONGRESS OF SERBIA
ACCREDITED AS INTERNATIONAL
3rd INTERNATIONAL CONGRESS
OF TMAS

OCTOBER 29th-31st, 2026
SAVA CENTER, BELGRADE, SERBIA

TEHNIČARSKI APSTRAKTI
TECHNICIAN ABSTRACTS

SAVA CENTAR / SAVA CENTER
Beograd, SRBIJA / Belgrade, Serbia
29–31. oktobar, 2026. / October 29th–31st, 2026

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USKLAĐIVANJE ORGANIZACIJE RADA TRANSFUZIOLOŠKE SLUŽBE U REPUBLICI SRBIJI U ODNOSU NA NOV ZAKON O TRANSFUZIJSKOJ MEDICINI

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Prema nekadašnjem principu, transfuziološka služba u Republici Srbiji je bila organizovana tako da je uključivala tri velika transfuziološka centra: Institut za transfuziju krvi Srbije (ITKS), Zavod za transfuziju krvi Vojvodine i Zavod za transfuziju krvi Niš. Takođe, u sistem su bile uključene 43 službe za transfuziju krvi pri zdravstvenim ustanovama i posebno Institut za transfuziologiju i hemobiologiju VMA. Sve navedene ustanove su bile odgovorne za prikupljanje krvi, pripremu komponenata, testiranje, kontrolu kvaliteta i distribuciju jedinica krvi i komponenata krvi.

Reorganizacija Službe transfuzije je započeta u okviru projekta Podrška EU Nacionalnoj službi za transfuziju krvi Srbije uz podršku Evropske agencije za rekonstrukciju i razvoj i Ministarstva zdravlja u periodu od 2003. do 2005. godine, sa ciljem poboljšanja i jačanja kapaciteta nacionalne Službe i iznalaženja načina za najoptimalniju reorganizaciju Službe.

Javna rasprava o Nacrtu zakona o transfuzionoj medicini sprovedena je od 22.01.2016. do 11.02.2016. godine, Zakon je usvojen 05.05.2017. godine, a u primeni je od 2018. Od novembra 2020. godine, a u skladu sa novim zakonom, u okviru ITKS je formiran Odsek za distribuciju krvi i komponenata krvi, koji vrši distribuciju krvi bolničkim bankama krvi u centralnom regionu i bolnickim bankama krvi na teritoriji grada Beograda.

Transfuziološka delatnost, u smislu ovog zakona, obuhvata planiranje, prikupljanje, testiranje, preradu krvi i komponenata krvi, kao i čuvanje, distribuciju i izdavanje krvi i komponenata krvi namenjenih transfuziji i obavlja se u ovlašcenim transfuzijskim ustanovama.

Klinička transfuzija, obuhvata delatnost čuvanja i izdavanja krvi i komponenata krvi za terapijsku primenu, pretransfuzijska testiranja, brigu za optimalnu primenu krvi i komponenata krvi, autolognu transfuziju, terapijske aferezne procedure i obavlja se u bolničkim bankama krvi.

U Republici Srbiji postoji 8 ovlašćenih transfuzijskih istanova: Institut za transfuziju krvi Srbije (ITKS), Zavod za transfuziju krvi Vojvodine, Zavod za transfuziju krvi Niš, Zavod za transfuziju krvi Kragujevac u osnivanju, Institut za trasfuziologiju i hemobiologiju VMA, Služba za transfuziju krvi KBC Zemun, Služba za transfuziju krvi OB Subotica, Služba za transfuziju krvi ZC Užice.

ITKS prikuplja krv na teritoriji grada Beograda izuzev Opstina Zemun i Surčin, Mačvanskom okrugu, Kolubarskom, Braničevskom, Podunavskom i delu Raškog okruga. NAT testiranje svih prikupljenih jedinica krvi na teritoriji Republike Srbije se obavlja u ITKS.

Reorganizacija usled usvajanja Zakna o transfuzijskoj medicini i podela delanosti transfuzijskih usanova omogućila je sa jedne strane jednak kvalitet i veću bezbednost svih prikupljenih jedinica krvi u Republici Srbiji, a sa druge starne u okviru bolničkih banaka krvi mogućnost za punu primenu *Patient Blood Management*-a, odnosno racionalnu primenu krvi i komponenata krvi i najadekvatnije transfuziološko zbrinjavanje pacijenata.

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ALIGNMENT OF THE ORGANIZATION OF THE TRANSFUSION SERVICE IN THE REPUBLIC OF SERBIA WITH THE NEW LAW ON TRANSFUSION MEDICINE

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Under the former organizational model, the transfusion service in the Republic of Serbia consisted of three major transfusion centers: the Serbian Blood Transfusion Institute (BTIS), the Blood Transfusion Service of Vojvodina, and the Blood Transfusion Service of Niš. In addition, the system included 43 blood transfusion services within healthcare institutions, as well as the Institute of Transfusiology and Hemobiology of the Military Medical Academy (MMA). All of these institutions were responsible for blood collection, component preparation, testing, quality control, and the distribution of blood and its components.

The reorganization of the transfusion service has began within the framework of the project *EU Support to the National Blood Transfusion Service of Serbia*, implemented with the support of the European Agency for Reconstruction and the Ministry of Health during the period 2003–2005. The project aimed to improve and strengthen the capacity of the national transfusion service and to identify the most effective model for its reorganization.

The public consultation on the Draft Law on Transfusion Medicine was conducted from January 22 to February 11, 2016. The Law was adopted on May 5, 2017, and has been in force since 2018. In November 2020, in accordance with the new Law, a Blood and Blood Components Distribution Department was established within the Blood Transfusion Institute of Serbia. This department is responsible for the distribution of blood and blood components to hospital blood banks in the central region of Serbia and to hospital blood banks within the territory of the City of Belgrade.

According to this Law, transfusion activities include the planning, collection, testing, processing, storage, distribution, and issuance of blood and blood components intended for transfusion, and are performed by authorized transfusion institutions.

Clinical transfusion practice includes the storage and issuance of blood and blood components for therapeutic use, pre-transfusion testing, ensuring the optimal use of blood and blood components, autologous transfusion, and therapeutic apheresis procedures. These activities are carried out in hospital blood banks.

There are currently eight authorized transfusion institutions in the Republic of Serbia: the Blood Transfusion Institute of Serbia (BTIS), the Blood Transfusion Service of Vojvodina, the Blood Transfusion Service of Niš, the Blood Transfusion Service of Kragujevac (in the process of establishment), the Institute of Transfusiology and Hemobiology of the Military Medical Academy, the Blood Transfusion Service of the Zemun Clinical Hospital Center, the Blood Transfusion Service of the General Hospital Subotica, and the Blood Transfusion Service of the Užice Health Center.

The Blood Transfusion Institute of Serbia collects blood in the territory of the City of Belgrade, excluding the municipalities of Zemun and Surčin, as well as in the Mačva, Kolubara, Braničevo, and Podunavlje districts, and part of the Raška District.

Nucleic Acid Testing (NAT) of all blood units collected in the Republic of Serbia is performed at the Serbian Blood Transfusion Institute.

The reorganization resulting from the adoption of the Law on Transfusion Medicine and the division of responsibilities among transfusion institutions has, on the one hand, ensured uniform quality standards and increased safety of all blood units collected in the Republic of Serbia. On the other hand, it has enabled hospital blood banks to fully implement Patient Blood Management (PBM), promoting the rational use of blood and blood components and providing the most appropriate transfusion care for patients.

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NOVA UREDBA EU O TVARIMA LJUDSKOG PODRIJETLA

D. Ratić

Uredba SoHO (Substance of Human Origin) regulira tvari ljudskog podrijetla namijenjene za ljudsku primjenu. Ova Uredba primjenjuje se na sve tvari dobivene iz ljudskog tijela bez obzira sadrže li stanice ili ne i jesu li te stanice žive ili ne, a koje uključuju područja krvi, tkiva, reproduktivnih stanica, humanog majčinog mlijeka, fekalnih mikrobiota i sve prerađene tvari namijenjene za ljudsku uporabu.

Dosadašnji regulatorni dokumenti EU, koji govore o krvi, tkivima i stanicama na snazi su više od dva desetljeća, te više ne odražavaju aktualno stanje. Transfuzijska medicina pokriva velik raspon aktivnosti: od rada na davalaštvu, obradi krvi, proizvodnji krvnih komponenti, laboratorijske znanosti, pa sve do bolesničke skrbi. To je jedna od rijetkih medicinskih djelatnosti koja objedinjuje znanost, tehnologiju, medicinu, javno zdravstvo i društvenu zajednicu u cjelini, te se uz automatizaciju i napredak u imunologiji i genetici i uz pojavu novih rizika vrlo brzo razvija.

Evaluacijom postojećih regulatornih akata Vijeće EU-a donijelo je nova pravila usmjerena na poboljšanje sigurnosti i kvalitete krvi, tkiva i stanica koje se upotrebljavaju u zdravstvenoj skrbi, te za olakšavanje njihova prekogranična opticaja u EU. Zaključeno je kako pacijenti i darivatelji nisu u potpunosti zaštićeni od rizika koji se mogu izbjeći, te kako za pacijente nije ostvaren puni potencijal inovativnih terapija.

Komisija EU je u srpnju 2022. nakon pregovora predložila novu SoHO Uredbu koja je nakon službenog usvajanja 17. srpnja 2024. objavljena u službenom glasilu EU (Uredba EU 2024/1938 Europskog parlamenta i Vijeća od 13. lipnja 2024. o standardima kvalitete i sigurnosti za tvari ljudskog podrijetla namijenjene primjeni kod ljudi i stavljanje izvan snage direktive 2002/23/EZ).

Nova SoHO Uredba zamjenjuje Direktive vezane uz krv, tkiva i stanice, obuhvaćene su sve SoHO namijenjene primjeni kod ljudi, te su obuhvaćene slične odredbe koje su ranije bile propisane u odvojenim zakonskim aktima, a obuhvaćeni su svi koraci od doniranja do primjene. Zakonodavstvo vezano uz organe ostaje nepromijenjeno.

Nova Uredba obvezuje sva SoHO tijela i subjekte na pridržavanje standarda najviše razine, koji su kao opći zahtjevi sadržani u Uredbi. U cilju postizanja najviših standarda, kada ne postoji zakonodavstvo EU kojim se opisuju potrebni postupci, radi njihove primjene usklađuju se kroz primjenu tehničkih smjernica EDQM (European Directorate for the Quallity of Medicines & Health Care) i ECDC (European Centre for Disease Prevencion and Control).

Primjena nove SoHO Uredbe stupa na snagu 7. kolovoza 2027. uz dodatnu godinu za neke odredbe.

Uredbom o tvarima ljudskog podrijetla osigurat će se prema najvišim standardima bolja zaštita darivatelja, primatelja i djece rođene nakon medicinski potpomognute oplodnje. Nova pravila usmjerena su na jačanje postojećeg pravnog okvira, te istodobno povećanje fleksibilnosti kako bi se održao korak sa znanstvenim i tehničkim razvojem. Temeljem nove Uredbe države članice mogu odlučiti da će primijeniti strože mjere za zaštitu svojih građana.

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ULOGA MEDICINSKOG TEHNIČARA U SPREČAVANJU NEŽELJENIH DOGAĐAJA KOD DOBROVOLJNIH DAVALACA KRVI

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Uvod Bezbednost dobrovoljnih davalaca krvi predstavlja jedan od osnovnih preduslova uspešnog funkcionisanja transfuzijske službe. Iako su neželjene reakcije tokom i nakon davanja krvi relativno retke i najčešće blagog intenziteta, njihova prevencija ima značajnu ulogu u očuvanju zdravlja davalaca i održavanju poverenja u sistem dobrovoljnog davalaštva krvi. Medicinski tehničari aktivno učestvuju u svim fazama procesa davanja krvi, od pripreme i informisanja davalaca do praćenja i evidentiranja eventualnih neželjenih događaja.
Cilj Prikazati značaj preventivnih mera u sprečavanju neželjenih događaja kod dobrovoljnih davalaca krvi i ulogu medicinskog tehničara u obezbeđenju bezbednog procesa davanja krvi.
Materijal i metod Izvršen je pregled dostupne stručne i naučne literature koja se odnosi na neželjene reakcije kod dobrovoljnih davalaca krvi, faktore rizika za njihov nastanak i preporučene mere prevencije. Analizirane su i smernice dobre transfuzijske prakse koje definišu postupke praćenja, dokumentovanja i upravljanja neželjenim događajima.
Rezultati Pregled literature ukazuje da se većina neželjenih reakcija kod davalaca može predupredi adekvatnom procenom zdravstvenog stanja davaoca, pravilnom pripremom pre davanja krvi, primenom mera hidratacije, obezbeđivanjem prijatnog okruženja i kontinuiranim nadzorom tokom postupka. Najčešće reakcije su vazovagalne prirode i blagog su intenziteta. Medicinski tehničari imaju ključnu ulogu u prepoznavanju faktora rizika, edukaciji davalaca, blagovremenom reagovanju u slučaju pojave reakcije i evidentiranju neželjenih događaja u pisanoj i elektronskoj dokumentaciji, čime se obezbeđuje sledljivost i kontinuirano unapređenje kvaliteta rada. Sistem kvaliteta i redovno praćenje pokazatelja neželjenih događaja omogućavaju analizu uzroka, prepoznavanje potencijalnih rizika i uvođenje korektivnih mera u cilju stalnog unapređenja bezbednosti davalaca krvi.
Zaključak Sistematična primena preventivnih mera značajno doprinosi smanjenju učestalosti neželjenih događaja kod dobrovoljnih davalaca krvi. Medicinski tehničari imaju važnu ulogu u očuvanju bezbednosti davalaca kroz edukaciju, nadzor, blagovremeno zbrinjavanje reakcija i adekvatno dokumentovanje svih događaja. Kontinuirana edukacija medicinskih tehničara i primena principa sistema kvaliteta predstavljaju osnovu za pravovremeno prepoznavanje i sprečavanje neželjenih događaja kao i za unapređenje bezbednosti i zadovoljstva dobrovoljnih davalaca krvi.

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THE ROLE OF MEDICAL TECHNICIANS IN PREVENTING ADVERSE EVENTS IN VOLUNTARY BLOOD DONORS

Introduction The safety of voluntary blood donors is one of the fundamental prerequisites for the successful functioning of transfusion services. Although adverse reactions during and after blood donation are relatively rare and usually mild in severity, their prevention plays a significant role in preserving donor health and maintaining confidence in the voluntary blood donation system. Medical technicians are actively involved in all phases of the donation process, from donor preparation and education to monitoring and recording potential adverse events.
Objective To present the importance of preventive measures in reducing adverse events among voluntary blood donors and to highlight the role of medical technicians in ensuring a safe blood donation process.
Material and methods A review of available scientific and professional literature related to adverse donor reactions, risk factors for their occurrence, and recommended preventive measures was conducted. In addition, guidelines of good transfusion practice defining procedures for monitoring, documenting, and managing adverse events were analyzed.
Results The literature review indicates that most adverse donor reactions can be prevented through adequate donor assessment, proper pre-donation preparation, hydration measures, a comfortable donation environment, and continuous monitoring during the donation process. The most common reactions are vasovagal in nature and generally mild in severity. Medical technicians play a key role in identifying risk factors, educating donors, responding promptly to adverse reactions, and documenting adverse events in both written and electronic records, thereby ensuring traceability and continuous quality improvement. Quality management systems and regular monitoring of adverse event indicators enable root-cause analysis, identification of potential risks, and implementation of corrective actions aimed at continuously improving donor safety.
Conclusion The systematic implementation of preventive measures significantly contributes to reducing the incidence of adverse events among voluntary blood donors. Medical technicians play an important role in maintaining donor safety through education, monitoring, timely management of adverse reactions, and appropriate documentation of all events. Continuous education of medical technicians and the application of quality management principles provide the foundation for the early recognition and prevention of adverse events, while contributing to improved donor safety and satisfaction.

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KONCENTRATI TROMBOCITA U ADITIVNOM RASTVORU PAS (PLATELET ADDITIVE SOLUTION) – ISKUSTVA ZAVODA ZA TRANSFUZIJU KRVI VOJVODINE

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Uvod: Savremena transfuzijska medicina usmerena je na unapređenje kvaliteta, bezbednosti i stabilnosti krvnih komponenata, uključujući koncentrate trombocita. Primena trombocitnog aditivnog rastvora PAS (Platelet Additive Solution) predstavlja značajan napredak u odnosu na čuvanje trombocita u isključivoj plazmi. PAS E generacije, reformulisan 2015. godine, omogućava bolje uslove skladištenja, smanjenje neželjenih reakcija i poboljšanu stabilnost trombocita tokom čuvanja.
Cilj rada: Cilj rada je prikaz iskustva Zavoda za transfuziju krvi Vojvodine u proizvodnji koncentrata trombocita u PAS aditivnom rastvoru i analiza kvaliteta proizvoda u skladu sa važećim evropskim smernicama.
Materijal i metode: Koncentrati trombocita proizvedeni su iz jedinica pune krvi dobrovoljnih davalaca. Nakon centrifugiranja i izdvajanja komponenata, dobijeni su trombocitni koncentrati koji su pulovani u PAS aditivni rastvor. Za jednu jedinicu proizvoda korišćena su četiri buffy coat koncentrata. Oko 70% plazme zamenjeno je PAS rastvorom. Sprovedene su kontrole kvaliteta, uključujući broj trombocita, pH vrednosti, titar ABO antitela i rezidulnih leukocita. Obrađeno je više od 200 koncentrata trombocita. Proces se kontinuirano prati u skladu sa važećim standardima i definisanim brojem kontrola.
Rezultati: Primena PAS aditivnog rastvora pokazala je stabilne pH vrednosti tokom skladištenja i zadovoljavajuće kvalitativne parametre u skladu sa evropskim standardima. Titar ABO antitela je smanjen, najčešće ispod 1:4–1:8, što doprinosi boljoj kompatibilnosti i smanjenju imunih reakcija. Prema podacima iz literature, primena PAS aditivnog rastvora povezuje se sa smanjenom učestalošću alergijskih i febrilnih nehemolitičkih transfuzionih reakcija, kao i potencijalnim smanjenjem rizika od TRALI reakcija. Kontinuirano praćenje kvaliteta se i dalje sprovodi kroz interne i eksterne kontrole.
Zaključak: Primena PAS aditivnog rastvora u proizvodnji koncentrata trombocita predstavlja značajan napredak u transfuzijskoj medicini. Ovaj pristup poboljšava stabilnost i bezbednost trombocitne komponente, unapređuje kompatibilnost ABO sistema i olakšava distribuciju. Iskustva Zavoda za transfuziju krvi Vojvodine potvrđuju da su PAS trombocitni koncentrati kvalitetna i bezbedna krvna komponenta u savremenoj praksi.
Ključne reči: PAS, Platelet Additive Solution, trombociti, krvne komponente, TRALI, transfuzijske reakcije, kontrola kvaliteta.

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PLATELET CONCENTRATES IN PLATELET ADDITIVE SOLUTION (PAS) – EXPERIENCE OF THE INSTITUTE FOR TRANSFUSION OF BLOOD OF VOJVODINA

Introduction: Modern transfusion medicine is focused on improving the quality, safety, and stability of blood components, including platelet concentrates. The use of Platelet Additive Solution (PAS) represents a significant advancement compared to storage of platelets exclusively in plasma. The PAS E generation, reformulated in 2015, provides improved storage conditions, reduced adverse reactions, and better platelet stability during storage.
Objective: To present the experience of the Institute for Transfusion of Blood of Vojvodina in the production of platelet concentrates in PAS additive solution and to analyze product quality in accordance with current European guidelines.
Material and Methods: Platelet concentrates were produced from whole blood units donated by voluntary donors. After centrifugation and component separation, platelet concentrates were obtained and subsequently pooled in PAS additive solution. Four buffy coat units were used per final product. Approximately 70% of plasma was replaced by PAS solution. Quality control included platelet count, pH values, ABO antibody titers, and residual leukocytes. More than 200 platelet concentrates were processed. The process is continuously monitored in accordance with defined standards and required control frequency per produced units.
Results: The use of PAS additive solution demonstrated stable pH values during storage and satisfactory quality parameters in accordance with European standards. ABO antibody titers were reduced, most commonly below 1:4–1:8, contributing to improved compatibility and reduced immune reactions. According to available literature, PAS use is associated with a reduced incidence of allergic and febrile non-hemolytic transfusion reactions, as well as a potential reduction in TRALI-related risk. Continuous quality monitoring is ongoing, with regular application of internal and external quality control procedures in line with regulatory requirements.
Conclusion: The use of PAS additive solution in platelet concentrate production represents a significant advancement in transfusion medicine. This approach improves platelet component stability and safety, enhances ABO compatibility, and supports efficient distribution logistics. Both institutional data and published literature confirm that PAS platelet concentrates represent a high-quality and safe blood component in modern transfusion practice.
Keywords: PAS, Platelet Additive Solution, platelets, blood components, TRALI, transfusion reactions, quality control.

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POTVRDNA TESTIRANJA DAVALACA KRVI NA MARKERE TRANSFUZIJOM PRENOSIVIH BOLESTI U 2025. GODINI U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE

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Potvrdna testiranja izvode se kod dobrovoljnih davalaca krvi koji imaju ponovno reaktivne rezultate osnovnog testa na markere transfuzijom prenosivih bolesti (TPB). **Cilj:** Prikaz i analiza rezultata potvrdnih testiranja na markere TPB u Institutu za transfuziju krvi Srbije u 2025.g. **Metod:** Analiza podataka je izvršena retrospektivnim uvidom u rezultate potvrdnog testiranja. Potvrdno testiranje primenjivano je za dokazivanje infekcije hepatitisa C, virusa humane imunodeficijencije i Sifilisa. Potvrdna testiranja rađena su uz upotrebu komercijalih „western blot“ testova Innolia score na aparatu Tendigo/Fujirebio, koji ima prateći softverski program za precizno tumačenje rezultata. **Rezultati:** U 2025 godini testirano je 76532 uzoraka davalaca krvi na markere TPB. Za 304 (0,39%) davaoca, koji su bili ponovo reaktivni nakon osnovnog testiranja urađena su potvrdna testiranja. Od ukupnog broja potvrdnih testiranja za hepatitis C je urađeno 120 (39,47%) testova, za virus humane imunodeficijencije 64 (21,06%), a za Sifilis 120 (39,47%). Za 16 uzoraka je dobijen potvrdno pozitivan rezultat na marker hepatitisa C (35,56%), 4 potvrdno pozitivanih rezultata na marker virusa humane imunodeficijencije (8,89 %), i 25 za Sifilis (55,55 %). **Zaključak:** Potvrđeno pozitivni rezultati su dobijeni za 45 uzoraka davalaca krvi što iznosi 14,80 % u odnosu na ukupan broj potvrdnih testiranja. Ustanovljeno je da je 0,05% testiranih davalaca pokazalo potvrđeno pozitivne rezultate na markere TPB, pri čemu je najzastupljeniji marker Sifilis. Potvrdna testiranja su vrlo značajna i neophodna u cilju rešavanja konačnog statusa davalaca krvi.
Ključne reči: markeri transfuzijom prenosivih bolesti, potvrdna testiranja, davaoci krvi

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CONFIRMATION TESTING OF BLOOD DONORS FOR MARKERS OF TRANSFUSION TRANSMITTED DISEASES IN THE BLOOD TRANSFUSION INSTITUTE OF SERBIA IN 2025.

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Confirmatory tests are performed in voluntary blood donors with repeated reactive results of screening test for markers of transfusion transmitted diseases. **Objective:** Presentation and analysis of the results of confirmatory tests for markers of transfusion transmit ted diseases at the Donor testing Department of Blood Transfusion Institute of Serbia in 2025. **Methods**: Data analysis was performed by retrospectively reviewing the results of confirmatory testing. Confirmatory testing was used to prove hepatitis C, human immunodeficiency virus and Syphilis infection. Confirmatory tests were performed using commercial Innolia score “western blot” tests on the Tendigo/Fujirebio device, with accompanying software program for accurate interpretation of the results. **Results:** In 2025. 76532 samples of blood donors were tested according to the national algorithm of screening testing for markers of transfusion transmitted diseases. For 304 (0,39%) donors, who were repeated reactive after screening testing, confirmatory tests were performed. Of the total number of confirmatory tests, 120 (39,47%) tests were performed for hepatitis C, 64 (21,06%) for human immunodeficiency virus, and 120 (39,47%) for Syphilis. Confirmed positive results were obtained for 45 blood donors, representing 14,80% of the total number of confirmatory tests. For 16 samples, positive result was obtained for the hepatitis C (35,56%), 4 positive results for the human immunodeficiency virus (8,89%), and 25 for Syphilis (55,55%). **Conclusion:** Confirmed positive results were obtained for 45 blood donors, representing 14,80% of the total number of confirmatory tests. It was determined that 0.05% of tested blood donors showed confirmed positive results for markers of transfusion transmitted diseases, and the most common marker is Syphilis. Confirmatory tests are very important and necessary in order to resolve the final status of blood donors.
Key words: transfusion transmitted diseases, confirmatory tests, blood donors

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DOPRINOS REGISTRA TIPIZIRANIH DAVALACA KRVI INSTITUTA ZA TRANSFUZIJU KRVI SRBIJE U EFIKASNIJEM ZBRINJAVANJU PACIJENATA TOKOM 2025

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Uvod: U Institutu za transfuziju krvi Srbije tokom 2012. godine prvi put su započete planske aktivnosti na formiranju Registra tipiziranih davalaca krvi Davaoci krvnih grupa O i A sa određenim fenotipskim karakteristikama u Rh sistemu se prema prethodno definisanim kriterijumima dodatno tipiziraju na antigene klinički značajnih krvnogrupnih sistema Registar tipiziranih davalaca Instituta za transfuziju krvi Srbije trenutno raspolaže podacima za 4900 dobrovoljnih davalaca krvi. **Cilj rada:** Analiza pretrage registra tipiziranih davalaca u cilju bržeg i lakšeg pronalaženja adekvatnih davalaca za pravovremeno transfuziološko zbrinjavanje imunizovanih pacijenata. **Metodologija:** Retrospektivna analiza zahteva upućenih za pretragu Registra tokom 2025 godine i analiza realizacije. **Rezultati:** U posmatranom periodu upućeno je 43 zahteva za pronalaženje adekvatnih davalaca iz registra, od toga 19 zahteva za pacijente kod kojih je detektovano jedno antitelo, 11 zahteva za pacijente sa 2 antitela, 4 zahteva za pacijente sa 3 antitela, 2 zahteva za pacijenta kod kojih je detektovano 4 antitela, jedan zahtev za pacijenta sa 5 antitela i 6 zahteva za pacijenta kod kojeg je detektovano 7 antitela. Po zastupljenosti kako pojedinačno, tako i udruženo, najčešće su prisutna antitela na antigene iz sistema Rh, Kidd, Duffy, Kell i MNS. Od 43 zahteva uspešno je zadovoljeno 42 (realizacija 97,67 %), te je za ove pacijente kroz Registar tipiziranih davalaca u navedenom periodu obezbeđeno 84 jedinice eritrocita. **Zaključak:** Postojanje Registra tipiziranih davalaca krvi od ključnog je značaja za blagovremeno i bezbedno lečenje pacijenata kojima je potrebna specifična transfuzija. Pretraga registra omogućava brzo pronalaženje odgovarajućih davalaca u hitnim i planiranim medicinskim zahvatima.
Ključne reči: Registar tipiziranih davalaca, imunizacija, antieritrocitna antitela, transfuzija eritrocita.

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CONTRIBUTION OF THE TYPED BLOOD DONORS REGISTER IN THE BLOOD TRANSFUSION INSTITUTE OF SERBIA TO MORE EFFICIENT PATIENT CARE IN 2025

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Backgroung: In 2012, the Blood Transfusion Institute of Serbia started planning activities for the first time, to establish the Typed Blood Donors Register. Donors of blood groups O and A with certain Rh phenotypic characteristics were additionally typed according to previously defined criteria on antigens of clinically significant blood systems Kell, Duffy, Kidd, MNS, Lewis and P1. The Typed Blood Donors Register of the Blood Transfusion Institute of Serbia currently has data for 4 900 voluntary blood donors. **Objective:** Analysis of the practical part of Typed Blood Donors Register searching in order to find adequate donors faster and easier for timely transfusion care of immunized patients. **Methodology:** Retrospective analysis of the requests for the register searching during the 2025, and analysis of the realization. **Results:** In the observed period, 43 requests were sent to find adequate donors from the registrer, of which 19 requests were for patients in whom one antibody was detected, 11 requests for patients with 2 antibodies, 4 requests for patients with 3 antibodies, 2 requests for patients with 4 antibodies, one request for a patient with 5 antibodies and 6 requests for a patient with 7 antibodies. Antibodies from the Rh, Kell, Duffy, Kidd and MNS are most often present, both individually or in combination. Out of the 43 requests, 42 were successful (97.67% realization), and 84 units of erythrocytes were provided for these patients through the Typed Blood Donor Register in the specified period. **Conclusion:** The existence of the Typed Blood Donor Register is of crucial importance for the timely and safe treatment of patients who require specific transfusion. Searching the register enables the rapid identification of suitable donors for emergency and planned medical procedures.
Keywords: Typed Blood Donor Register, immunization, anti-erythrocyte antibodies, erythrocyte transfusion

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A, PARABOMBAY, RETKA PODGRUPA ABO SISTEMA-PRIKAZ SLUČAJA.

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Uvod: Pored uobičajene distribucije krvnih grupa u okviru sistema ABO (A, B, AB i O) postoje i osobe sa veoma retkim fenotipovima, čija je učestalost u celom svetu manja od 1%.

Prikaz slučaja: Na Odeljenju za imunohematološka ispitivanja ITKS, 2024. godine otkriven je slučaj retkog A, paraBombay fenotipa sa anti-HI antitelom u serumu trudnice, u prvoj trudnoći. U rutinskom određivanju krvne grupe na aparatu IH-500, metodom u gelu, rezultat je pokazao negativan nalaz u ispitivanju eritrocita sa poznatim ABO test serumima, a aglutinaciju jačine 4+ sa B test eritrocitima i plazmom. Ispitivanje manuelnim metodom na ID karticama, uz dodatak enzima bromelina, dalo je slabu aglutinaciju sa anti-A (± do 1+) test reagensom. Manuelna metoda ispitivanja ABO krvne grupe u epruveti dala je slab nalaz sa anti-A (±) i nešto jači sa anti-A,B (1+) test reagensima. Lewis fenotip je bio Le(a-b+), dok je ispitivanje eritrocita sa anti-A_1 i anti-H lektinima pokazalo negativan nalaz. Ispitivanje plazme pokazalo je prisustvo anti-HI antitela (ABO test eritrocitima "in house" proizvodnja ITKS, kao i O, RhD-pozitivnim eritrocitima neonatusa).Molekularna genotipizacija ukazala je na mogućnost postojanja A1 alele. Referentna imunohematološka laboratorija u Bristolu je potvrdila da se radi o fenotipu paraBombay, O_h^A-sekretoru, bez prisustva H supstance na eritrocitima i postojanjem anti-H "like" antitela u plazmi.

Zaključak: Precizno i tačno utvrđivanje ABO krvne grupe značajno je u prevenciji neželjenih transfuzionih reakcija i sprovođenju bezbedne transfuzije krvi. Potvrđen je i značaj timskog rada i stručne međulaboratorisjke i multidisciplinarne saradnje u zbrinjavanju pacijenata.

Ključne reči: ABO podgrupe, paraBombay, multidisciplinarna saradnja

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A, PARABOMBAY , A RARE SUBGROUP OF THE ABO SYSTEM -CASE REPORT

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Introduction: In addition to the usual distribution of ABO blood groups(A, B, AB and O) there are also people with very rare types, whose frequency is, globally, less than 1%.

Case report: In 2024, a case of rare A, paraBombay phenotype with anti-HI antibody in the serum of a pregnant woman, in her first pregnancy, was discovered at the Department of tmmunohematological testing at BTIS. In the routine determination of the ABO/RhD blood group on the IH-500 device, using the gel method, the result showed a negative finding in the examination of red cells with known ABO test reagents, and agglutination strength of 4+ with B test red cells and plasma. Manual testing on ID cards, with the addition of bromelain enzyme, gave weak agglutination with the anti-A (± to 1+) test reagent. The manual method in a test tube gave the weak result with anti-A (±) and a slightly stronger one with anti-A,B (1+) test reagents. The Lewis phenotype was Le(a-b+), while the red cell typing with anti-A1 and anti-H lectins showed a negative finding. Plasma testing showed the presence of anti-HI antibodies ("in house" production of ABO test red cells in BTIS, as well as O, RhD-positive red cells of neonates). Molecular genotyping indicated the possibility of the existence of the A1 allele. The reference immunohematology laboratory in Bristol confirmed a paraBombay phenotype, an O_hA-secretor, without the presence of substance H on red cells and the existence of anti-H "like" antibodies in the plasma.

Conclusion: Precise and accurate determination of ABO blood group is important in the prevention of adverse transfusion reactions and the implementation of safe blood transfusion. The importance of teamwork and professional interlaboratory and multidisciplinary cooperation in patient care was also confirmed.

Key words: ABO subgroups, paraBombay, multidisciplinary collaboration

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TEHNIČKI KVAROVI LABORATORIJSKE OPREME: IZAZOVI I ISKUSTVA MEDICINSKOG OSOBLJA U TRANSFUZIJSKOJ DJELATONOSTI

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UVOD: Kvalitetno i blagovremeno pružanje usluge, kontinuitet i sigurnost u radu, tehnička efiksnost i pouzdanost medicinske opreme skupa predstavljaju preduslov za uspješan rad transfuzijske laboratorije. U savremenim transfuzijskim laboratorijama adekvatna tehnička podrška, preventivno i blagovremeno djelovanje, osposobljenost osoblja u velikoj mjeri mogu uticati na organizaciju i kvalitet rada, te predstavljaju jedan od najvećih izazova u današnjoj transfuzijskoj djelatnosti.

CILJ RADA: Prikazati iskustva medicinskog osoblja kroz analizu tehničkih kvarova laboratorijske i prateće opreme, njihovu ulogu u sprovođenje procedura pri prepoznavanju, prijavljivanju i rješavanju određenih situacija, kao i spremnost na improvizaciju i pravovremeno djelovanje.

MATERIJAL I METODE: Fenomenološka analiza iskustva osoblja iz svakodnevne laboratorijske prakse s primarnim osvrtom na upravljanje kvarovima i njihov uticaj na organizaciju rada i radne procese, a usljed ovisnosti procesa o automatizaciji, digitalizaciji i informatizaciji.

REZULTATI: Analizom iskustva osoblja Odjeljenja za imunohematološko testiranje uviđamo različite izazove tehničke prirode, a možemo ih podijeliti na hardverske, softverske i infrastrukturne. Najčešći problemi uključuju zastoje analizatora, greške u operativnim aplikacijama, kvarove medicinskih i drugih rashladnih uređaja, prekide u napajanju i dr.

ZAKLJUČAK: Da bi osigurali kvalitet, sigurnost i pouzdanost laboratorijskih procesa neophodna je efikasna politika preventivnog djelovanje putem nabavke kvalitetne, redovnog servisiranja opreme, dobre saradnje sa ovlaštenim servisima, osposobljenosti i agilnosti tehničkog osoblja, efektivno upravljanje tehničkim izazovima i kvarovima od strane medicinskog osoblja **što** u savremenim laboratorijskim operacijama zahtijeva kontinuiranu i strukovno-tehnički zahtjevnu edukaciju.

KLJUČNE RIJEČI: automatizacija, process, podrška.

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TECHNICAL FAILURES OF LABORATORY EQUIPMENT: CHALLENGES AND EXPERIENCES OF MEDICAL STAFF IN TRANSFUSION MEDICINE

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INTRODUCTION: High-quality and timely service, continuity and safety of operations, technical efficiency and reliability of medical equipment, together constitute essential prerequisites for the successful functioning of a transfusion laboratory. In transfusion laboratories, adequate technical support, preventive and timely interventions, and well-trained personnel can significantly influence work quality, representing challenges in transfusion practice.

OBJECTIVE: To present the experiences of medical personnel through an analysis of technical failures of laboratory equipment, their role in implementing procedures for identifying, reporting, and resolving specific situations, as well as their readiness to improvise and respond promptly.

MATERIALS AND METHODS: A phenomenological analysis of experiences from routine laboratory practice was conducted, with a primary focus on fault management and its impact on work organization and operational processes, particularly considering the increasing dependence of laboratory activities on automation, digitalization, and information technology systems.

RESULTS: An analysis of the experiences of staff working in the Immunohematology Testing Department revealed various technical challenges, which can be categorized as hardware-related, software-related, and infrastructure-related. The most common issues included analyzer malfunctions, software applications issues, failures of medical and other refrigeration equipment, power supply interruptions, and similar incidents.

CONCLUSION: Ensuring the quality, safety, and reliability of laboratory processes requires an effective preventive maintenance policy through the procurement of high-quality equipment, regular servicing, cooperation with service providers, competence and agility of technical personnel. Effective management of technical challenges and equipment failures by medical staff is also essential and, in modern laboratory operations, requires continuous and professionally demanding technical education.

KEYWORDS: automation, process, support.

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NEŽELJENE TRANSFUZIJSKE REAKCIJE – PETOGODIŠNJE ISKUSTVO JEDNOG TRANSFUZIJSKOG CENTRA

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Uvod: Transfuzijske reakcije predstavljaju neželjene komplikacije povezane sa primenom komponenata krvi i mogu biti blage do ozbiljne, akutne ili odložene. Svaka sumnja na neželjenu reakciju zahteva prekid transfuzije i sprovođenje odgovarajuće laboratorijske obrade radi utvrđivanja uzroka i razlikovanja hemoliznih od nehemoliznih reakcija. Uloga imunohematološke laboratorije je ključna u obradi i interpretaciji dobijenih rezultata.

Cilj: Prikazati petogodišnje iskustvo laboratorije u obradi neželjenih transfuzijskiih reakcija, sa osvrtom na najčešće laboratorijske nalaze i postupke dijagnostičke obrade.

Metode: Urađena je retrospektivna analiza prijavljenih sumnji na neželjene reakcija u periodu od pet godina. Laboratorijska obrada obuhvatila je određivanje krvne grupe ABO/RhD, skrining antitela metodom indirektnog antiglobulinskog testa (IAT), direktan antiglobulinski test (DAT) i test interreakcije iz pretransfuzijskog i posttransfuzijskog uzorka, metodom u gelu, uz dodatna ispitivanja u zavisnosti od vrste primenjene komponente.

Rezultati: U petogodišnjem periodu prijavljeno je 20 slučajeva neželjenih reakcija na transfuziju komponenata krvi. Najveći broj bio je povezan sa transfuzijom eritrocita (9/20), bez laboratorijskih znakova hemolize, sa blagom kliničkom slikom. Reakcije nakon primene ZSP prijavljene su kod 4 pacijenta, dok je 5 pacijenata imalo reakcije nakon transfuzije trombocita, pretežno alerigijske prirode. Zabeležena je jedna sumnja na TRALI, koji nije dokazan. Jedan pacijent imao je reakciju nakon uzastopne primene komponenti eritrocita i ZSP.

Zaključak: U analiziranom petogodišnjem periodu većina prijavljenih reakcija bila je blagog kliničkog toka. Pravovremena i standardizovana laboratorijska obrada neželjenih transfuzijskih reakcija omogućila je utvrđivanje uzroka reakcije i doprinela bezbednijem transfuzijskom lečenju.

Ključne reči: transfuzijske reakcije, hemovigilanca, pretransfuziona testiranja

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ADVERSE TRANSFUSION REACTIONS: A FIVE-YEAR EXPERIANCE OF A SINGLE TRANSFUSION CENTER

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Introduction: Transfusion reactions are adverse events associated with the administration of blood components and may range from mild to severe, occuring as acute and delayed. Any suspected transfusion reaction requires immediate discontinuation of the transfusion and appropriate laboratory investigation to determine the underlying cause and to distinguish hemolytic from non-hemolytic reactions. The immunohematology laboratory plays a key role in the evaluation and interpretation of laboratory findings.

Aim: To present the five-years experiance of our laboratory in the investigation of adverse transfusion reactions, with emphasis on the most common laboratory findings and diagnostic procedures.

Material and Methods: A retrospective analysis of reported suspected reactions over a five-year period was performed. Laboratory investigations included ABO/Rh blood group determination, antibody screening using the indirect antiglobulin test (IAT), the direct antiglobulin test (DAT), and crossmatching using both pre- and post-transfusion patient samples by the gel method, with additional investigations performed according to the type of transfused blood component.

Results: During the five-year study period, 20 suspected transfusion reaction were reported. Most reactions were associated with red blood cell transfusions (9/20), without laboratory evidence of hemolysis and with mild clinical manifestations. Four reactions occured following fresh frozen plasma transfusion, while five patients developed reactions after platelet transfusion, predominantly allergic. One suspected case of transfusion-related acute lung injury (TRALI) was investigated but not confirmed. One patient experianced reactions following transfusions of both red blood cells and fresh frozen plasma.

Conclusion: During five-year period, most reported transfusion reactions were clinically mild. Standardized laboratory investigation of suspected transfusion reactions enabled accurate diagnosis and contributed to safer transfusion practice.

Key words: Transfusion reactions, hemovigilance, pretransfusion testing

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SCREENING AND CONFIRMATORY TESTING RESULTS FOR HEPATITIS C AMOUNG VOLUNTARY BLOOD DONORS AT THE BLOOD TRANSFUSION INSTITUTE OF SERBIA IN 2025

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Introduction: Hepatitis C remains a major public health concern due to its potential to cause chronic liver disease, cirrhosis, and hepatocellular carcinoma. Screening voluntary blood donors for anti-HCV antibodies is an integral part of mandatory blood donation testing to ensure transfusion safety. Reactive screening results require confirmatory testing to verify or exclude HCV infection. Aim: To present the results of screening and confirmatory testing for hepatitis C amoung voluntary blood donors at the Blood Transfusion Institute of Serbia during 2025. Materials and Methods: A retrospective analysis was performed on samples with initially reactive anti-HCV screening results. During 2025, a total of 76,532 samples were tested, including 73,706 whole blood donors and 2,826 platelet apheresis donors. Screening was performed using chemiluminescent microparticle immunoassay (CMIA) and enzyme-linked immunosorbent assay (ELISA), while confirmatory testing was carried out using the Inno-Lia HCV Score immunoblot assay (Fujirebio). Results: Of the 76,532 tested samples, 108 (0.14%) were initially reactive. Repeat testing in duplicate confirmed reactivity in 95 samples (87.9% of initially reactive semples; 0.12% of all tested samples), which were subsequently referred for confirmatory testing. Confirmed positive results were obtained in 16 donors (16.8% of repeatedly reactive samples; 0.02% of all tested samples), while 17 donors (17.9%) had indeterminate results requiring repeat testing after six months. Following completion of the diagnostic workup, donors were informed of their results, received appropriate counseling, and when indicated, were referred for further evaluation and treatment. Conclusion: Confirmatory testing enables differentiation between true-positive and falsely reactive screening results, preventing unnecessary permanent deferral of blood donors and representing an essential component of transfusion safety. In addition, it facilitates the early detection of HCV infection and timely referral of infected individuals for further evaluation and treatment.

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SAVREMENA IMUNOHEMATOLOŠKA DIJAGNOSTIKA FETALNE I NEONATALNE ALOIMUNE TROMBOCITOPENIJE

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Uvod: Patogeneza fetalne i neonatalne aloimune trombocitopenije (FNAIT) je slična patogenezi hemolizne bolesti fetusa i novorođenčeta (HBFN). Nakon transplacentarnog transporta At se vezuju za odgovarajući antigen, što može dovesti do destrukcije trombocita i supresije trombocitopoeze. Dijagnoza FNAIT obuhvata genotipizaciju majke, oca i deteta i dokazivanje specifičnog antitrombocitnog At u plazmi.
Metod: Urađena je retrospektivna analiza podataka iz protokola Odeljenja za imunohematološka ispitivanja (ITKS) od januara 2021. do juna 2026. godine. Izolacija DNK je rađena QIAamp DNA Blood Mini Kit QIAGEN Hilden, Nemačka. Genotipizacija je rađena FluoGene metodom (modifikovani SSP PCR) na aparatu FluoVista analyzer Inno-train Diagnostik GmbH Kronberg Nemačka, odnosno real time PCR na aparatu FluoQube, testovima HPA-FluoGene i HPA-FluoGeneNX Inno-train Diagnostik GmbH Kronberg Nemačka. Rađena je genotipizacija za osam HPA sistema (HPA-1 do HPA-6, HPA-9 i HPA-15).
Rezultati: Genotipizirano je 53 para majka-dete. U 26 (49%) slučaja analizirana je DNK fetusa iz uzorka krvi dobijenog kordocentezom. Kod 25 (47%) parova nije dokazana inkompatibilija. Kod parova sa dokazanom inkompatibilijom bilo je 14 (50%) koji su bili inkompatibilni u jednom sistemu, 11 (39%) sa inkompatibilijom u dva i 3 (11%) para sa inkompatibilijom u tri sistema. Najčešće je detektovana inkompatibilija u sistemu HPA-15 kod 13 parova. Slede sistemi HPA-1 i HPA-3 sa po 12 dokazanih inkompatibilija. Za sisteme HPA-4, -6 i -9 nisu dokazani slučajevi inkompatibilije.
Zaključak: Učestalosti inkompatibilija saglasne su sa poznatim frekvencijama HPA alela u evropskim populacijama u kojima je FNAIT najčešće uzrokovan imunizacijom u sistemima HPA-1, -3 i -15. Laboratorijsku dijagnostiku FNAIT treba tumačiti u skladu sa postojećom kliničkom slikom.
Ključne reči: HPA, FNAIT, genotipizacija

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CURRENT IMMUNOHAEMATOLOGICAL DIAGNOSIS OF FETAL AND NEONATAL ALLOIMMUNE THROMBOCYTOPENIA

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Introduction: The pathogenesis of fetal and neonatal alloimmune thrombocytopenia (FNAIT) is similar to the pathogenesis of haemolytic disease of the fetus and newborn (HBFN). After transplacental transport, antibodies (Abs) are bound to the corresponding antigen, what can lead to destruction of platelets and suppression of thrombocytopoiesis. The diagnosis of FNAIT includes the genotyping of the mother, father and child and the demonstration of specific antiplatelet Abs in the plasma.
Method: A retrospective analysis of data from the protocol of the Department for Immunohematological Testing (BTIS) from January 2021 to June 2026 was performed. DNA isolation was performed with QIAamp DNA Blood Mini Kit QIAGEN Hilden, Germany. Genotyping was performed using the FluoGene method (modified SSP PCR) on the FluoVista analyzer Inno-train Diagnostik GmbH Kronberg Germany, i.e. real time PCR on the FluoQube apparatus, HPA-FluoGene and HPA-FluoGeneNX tests Inno-train Diagnostik GmbH Kronberg Germany. Genotyping was performed for eight HPA systems (HPA-1 to HPA-6, HPA-9 and HPA-15).
Results: 53 mother-child pairs were genotyped. In 26 (49%) cases, fetal DNA was analyzed from a blood sample obtained by cordocentesis. Incompatibility was not proven in 25 (47%) couples. In couples with proven incompatibility, there were 14 (50%) who were incompatible in one system, 11 (39%) with incompatibility in two and 3 (11%) couples with incompatibility in three systems. Most often, incompatibility was detected for the HPA-15 system in 13 couples. Next are the HPA-1 and HPA-3 systems with 12 proven incompatibilities each. No cases of incompatibility have been proven for the HPA-4, -6 and -9 systems.
Conclusion: Incompatibility frequencies are consistent with known HPA allele frequencies in European populations where FNAIT is most commonly caused by immunization in the HPA-1, -3, and -15 systems. Laboratory diagnostics of FNAIT should be interpreted in accordance with the existing clinical picture.
Key words: HPA, FNAIT, genotyping

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ULOGA INTEGRISANOG SISTEMA KVALITETA U PRAĆENJU I OČUVANJU ZDRAVLJA DOBROVOLJNIH DAVALACA KRVI

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Uvod Integrisani sistem upravljanja kvalitetom u Zavodu za transfuziju krvi Vojvodine zasniva se na standardima ISO 9001 i ISO 14001, kao i na zahtevima Zakona o transfuzijskoj delatnosti i principima hemovigilance. Kontinuirano unapređenje kvaliteta obuhvata praćenje svih procesa, od selekcije davaoca do distribucije krvnih komponenti, uz primenu dobre laboratorijske i dobre proizvođačke prakse.
Cilj Cilj rada je da prikaže značaj sistema kontrole kvaliteta u očuvanju zdravlja dobrovoljnih davalaca krvi kroz kontinuirano laboratorijsko praćenje i stručnu komunikaciju sa davaocima.
Materijal i metode Sve jedinice krvi i pripadajući uzorci testirani su na zakonom propisane parametre. U okviru Službe za obezbeđenje i kontrolu kvaliteta formirana je savremeno opremljena biohemijsko-hematološka laboratorija koja omogućava praćenje zdravstvenog stanja davalaca i kontrolu kvaliteta krvnih komponenti. Pored obaveznih analiza, sprovode se biohemijska, hematološka i hemostazna ispitivanja kod davalaca tokom redovnih akcija dobrovoljnog davanja krvi, kao i kod osoba sa sniženim hemoglobinom, sumnjom na infekciju ili drugim odstupanjima u laboratorijskim nalazima.
Rezultati Mesečno se izvrši više od 3.000 dodatnih laboratorijskih analiza. Prate se parametri biohemijskog statusa (glukoza, urea, kreatinin, gvožđe, feritin, lipidni status, CRP i dr.), kompletna krvna slika i parametri hemostaze. Dobijeni rezultati pokazuju da dobrovoljni davaoci krvi predstavljaju pretežno zdravu populaciju, uz statistički zanemarljiv procenat odstupanja (<1%). U slučajevima patoloških nalaza davaoci se blagovremeno upućuju na dalje dijagnostičko ispitivanje i lečenje. Direktna komunikacija sa davaocima omogućava pružanje stručnih saveta i dodatno doprinosi očuvanju njihovog zdravlja.
Zaključak Kontrola kvaliteta i kontinuirano praćenje zdravstvenog stanja davalaca predstavljaju važan segment hemovigilance i transfuzijske bezbednosti. Očuvanje zdravlja i zadovoljstva davalaca doprinosi njihovom ponovnom dolasku, obezbeđivanju stabilnih zaliha krvi i sigurnosti pacijenata kojima je transfuzija neophodna.
Ključne reči: hemovigilansa, integrisani sistem kvaliteta, dobrovoljni davaoci krvi

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THE ROLE OF AN INTEGRATED QUALITY MANAGEMENT SYSTEM IN MONITORING AND PRESERVING THE HEALTH OF VOLUNTARY BLOOD DONORS

Introduction The integrated quality management system at the Blood Transfusion Institute of Vojvodina is based on ISO 9001 and ISO 14001 standards, as well as the requirements of the Law on Transfusion Medicine and the principles of haemovigilance. Continuous quality improvement includes monitoring all processes, from donor selection to blood component distribution, in accordance with Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP).
Objective The aim of this study was to demonstrate the importance of the quality control system in preserving the health of voluntary blood donors through continuous laboratory monitoring and professional communication with donors.
Materials and Methods All blood units and corresponding samples were tested for legally required parameters. Within the Quality Assurance and Quality Control Department, a modern biochemical and hematological laboratory was established, enabling continuous monitoring of donor health and quality control of blood components. In addition to mandatory testing, biochemical, hematological, and hemostatic analyses are performed during regular blood donation campaigns, as well as in donors with low hemoglobin levels, suspected infections, or other abnormal laboratory findings.
Results More than 3,000 additional laboratory analyses are performed monthly. Monitored parameters include biochemical markers (glucose, urea, creatinine, iron, ferritin, lipid profile, C-reactive protein, etc.), complete blood count, and hemostatic parameters. The obtained results indicate that voluntary blood donors represent a predominantly healthy population, with a statistically negligible proportion of abnormalities (<1%). Donors with pathological findings are promptly referred for further diagnostic evaluation and treatment. Direct communication with donors enables the provision of professional advice and recommendations, further contributing to the preservation of their health.
Conclusion Quality control and continuous monitoring of donor health represent important components of haemovigilance and transfusion safety. Preserving donor health and satisfaction contributes to repeat donations, ensures a stable blood supply, and enhances the safety of patients requiring transfusion therapy.
Keywords: haemovigilance, integrated quality management system, voluntary blood donors

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BACTERIAL SCREENING OF PLATELET CONCENTRATES USING THE BACT/ALERT SYSTEM – THE NURSING ROLE IN ENSURING QUALITY AND SAFETY OF THE TRANSFUSION PROCESS: EXPERIENCE OF THE TRANSFUSION CENTER, UNIVERSITY CLINICAL HOSPITAL MOSTAR, BOSNIA AND HERZEGOVINA

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1. Introduction Bacterial contamination of platelet concentrates remains one of the most significant infectious risks in transfusion medicine. Unlike other blood components, platelet concentrates are stored at room temperature (20–24°C) under continuous agitation to preserve their functional viability. These storage conditions, while necessary for platelet survival, simultaneously provide an optimal environment for bacterial proliferation. Consequently, even minimal contamination during collection, processing, or storage may lead to rapid bacterial growth and potentially severe transfusion-transmitted infections. Although transfusion-transmitted bacterial infections have become relatively rare due to modern safety measures, they are still associated with considerable morbidity and mortality. Clinical manifestations may range from mild febrile reactions to severe septic shock. Therefore, continuous improvement of bacterial detection strategies remains an essential component of transfusion safety programs worldwide. In recent years, automated culture systems such as BacT/ALERT have become the standard method for bacterial screening of platelet components. These systems enable continuous monitoring of microbial growth through the detection of changes in carbon dioxide (CO_2) production, allowing early identification of contaminated units before clinical use. Within this context, the role of nurses in transfusion medicine has become increasingly important. In addition to participating in transfusion practice, nurses play a key role in the pre-analytical and laboratory phases of blood component processing. Their responsibilities include strict adherence to aseptic techniques, accurate sample identification, proper labeling, maintenance of traceability, documentation, and timely communication with laboratory personnel.
2. Aim The aim of this study was to evaluate the results of routine bacterial screening of platelet concentrates using the BacT/ALERT system in a tertiary transfusion center and to emphasize the importance of nursing professionals in ensuring quality, safety, and traceability throughout the transfusion process.
3. Materials and Methods A retrospective observational study was conducted at the Transfusion Center of the University Clinical Hospital Mostar, Bosnia and Herzegovina, between 16 April and 19 June 2026.
All platelet concentrates prepared and issued during the study period were included. These comprised both pooled platelet concentrates prepared using the buffy coat method and apheresis platelet concentrates. Each unit underwent routine bacterial screening using the BacT/ALERT automated microbial detection system.
3.1 Sample Processing
Samples were collected under strict aseptic conditions. Nursing staff played a central role in the pre-analytical phase through: verification of donor and product identification, preparation of sterile materials and culture bottles, aseptic sample collection, inoculation of samples into aerobic and anaerobic BacT/ALERT culture bottles, correct labeling and barcoding of samples, ensuring complete traceability throughout the process Following inoculation, culture bottles were loaded into the BacT/ALERT system and incubated according to the manufacturer's instructions and internal laboratory protocols.
3.2 Detection and Monitoring The BacT/ALERT system continuously monitored culture bottles for microbial growth by detecting changes in CO_2 production. Positive signals triggered automated alerts and immediate notification of laboratory personnel. In the event of a positive result, confirmatory microbiological procedures were performed, including subculture on appropriate media, Gram staining, and microorganism identification using standard laboratory methods.
3.3 Data Collection and Analysis The following parameters were analyzed: total number of platelet concentrates tested number and percentage of positive results time to detection of bacterial growth results of confirmatory microbiological testing. Descriptive statistical methods were used for data analysis.
4. Results During the study period, a total of 234 platelet concentrates were screened using the BacT/ALERT system. Of all tested units, one positive result was detected, corresponding to a positivity rate of 0.43%. The positive signal was identified on the sixth day of incubation in an anaerobic culture bottle. The implicated unit was immediately withdrawn from potential clinical use and referred for further microbiological investigation, including pathogen identification and confirmatory testing. All remaining platelet concentrates tested negative for bacterial contamination and were considered safe for transfusion according to institutional protocols. No additional positive findings or clustering of contamination events were observed during the study period.
5. Discussion The results of this study demonstrated a very low rate of bacterial contamination among platelet concentrates screened using the BacT/ALERT system. The observed positivity rate of 0.43% is consistent with findings reported in the literature, indicating that modern bacterial screening methods significantly reduce the risk of transfusion-transmitted bacterial infections.
The detection of a single positive result on the sixth day of incubation in an anaerobic culture bottle raises important considerations regarding the nature of contamination. Late positivity may be associated with low-level bacterial contamination, slow-growing microorganisms, or possible pre-analytical contamination during sample collection. Therefore, confirmatory microbiological testing is essential to distinguish true contamination from procedural artefacts. The pre-analytical phase represents a critical component of transfusion safety, as most errors occur during this stage. In this study, nursing professionals were directly involved in all key pre-analytical procedures. Their responsibilities included strict adherence to aseptic techniques, accurate sample identification, correct labeling, and maintenance of traceability. The implementation of the BacT/ALERT system has significantly improved the detection of contaminated platelet units and enhanced patient safety. However, technology alone is insufficient. Its effectiveness depends largely on the quality of human performance, particularly in the pre-analytical phase, where nurses play a decisive role.
6. Conclusion Routine bacterial screening of platelet concentrates using the BacT/ALERT system demonstrated a very low rate of bacterial contamination in the studied population. The findings confirm the effectiveness of automated culture-based screening in ensuring the microbiological safety of platelet components. The nursing role is fundamental throughout all stages of the transfusion process, particularly in aseptic sampling, labeling, traceability, documentation, and communication with laboratory services. High levels of nursing competence directly contribute to the prevention of transfusion-related complications and to overall blood component quality assurance. The combination of advanced automated systems and skilled nursing practice represents a key element of modern transfusion safety strategies and should continue to be supported through education, training, and adherence to standardized protocols.

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REZULTATI UČEŠĆA U SPOLJAŠNJIM KONTROLAMA ZA KRVNE SLIKE I KVALITET KOMPONENATA KRVI U PERIODU OD 2021. DO 2025. GODINE

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Uvod: Krvna slika je najčešća laboratorijska analiza i od rezultata zavisi da li osoba može da bude davalac krvi ili komponente krvi, a u slučaju pacijenta zavisi dalja dijagnostika ili lečenje. Određivanje pojedinih parametara iz krvne slike deo je rutinske kontrole kvaliteta u proizvodnji komponenata krvi. **Cilj:** Prikaz rezultata spoljašnjih kontrola za krvne slike i kvalitet komponenata krvi. **Materijal i metode:** U periodu od 2021. do 2025. godine u okviru programa UKNEQAS Haematology iz Watforda, Velika Britanija, ispitano je 120 uzorka krvnih slika odnosno 480 parametara: leukociti (WBC), eritrociti (RBC), hemoglobin (Hb) i broj trombocita (PLT). Takođe su ispitana 36 uzoraka komponenti eritrocita za parametre Hb i Hct i **36** uzoraka komponenti trombocita za parametar PLT. Svi uzorci su bili iz humane krvi dobijeni u tečnom stanju. Analize su urađene na hematološkom analizatoru HORIBA ABX Micros ES 60. Dobijeni rezultati su od strane organizatora upoređivani sa rezultatima drugih učesnika i predstavljeni preko indeksa devijacije (DI) što je identično Z-skoru. **Rezultati:** Od parametara za krvne slike 31 (6.5%) rezultat je bio van konsenzusa i neprihvatljiv - 8 (1.7%) rezultata leukocita i 23 (4.8%) rezultata trombocita. Od parametara za komponente krvi su 3 rezultata trombocita (8,3%) bila van konsenzusa i prihvatljiva., a 1 (2,7%) rezultat hemoglobina i 1 (2,7%) hematokrita su bili van konsenzusa i neprihvatljivi. **Zaključak:** Rezultati 449 (93,5%) parametara krvnih slika i 31 (86,3%) su bili u konsenzusu. Najčešći parametri van konsenzusa su bili trombociti, posebno uzorci sa smanjenim brojem trombocita. Varijabilnost u rezultatima van konsenzusa je povezana sa kašnjenjem uzoraka, posebno za vreme pandemije COVID-19 što je značajno uticalo na brojanje trombocita metodom impendance.. Vreme i način transporta i oscilacije u temperaturi utiču na rezultate, posebno leukocita i trombocita, na šta treba obratiti pažnju u spoljašnjim kontrolama, i u svakodnevnom radu sa uzorcima.

Ključne reči: spoljašnja, kvalitet, kontrola, krvne slike, komponente krvi

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RESULTS FROM EXTERNAL QUALITY ASSESSMENT SCHEME FOR COMPLETE BLOOD COUNT AND BLOOD COMPONENT QUALITY FROM 2021 TO 2025

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Introduction: Complete blood count (CBC) is the most commonly performed laboratory analysis and its results determine whether a person is eligible to be a blood or blood component donor, while in patients the results influence further diagnostics or treatment. Determination of certain CBC parameters is part of routine quality control in blood component production. **Aim:** To present the results of external quality assessment for complete blood counts and blood component quality. **Material and Methods:** From 2021 to 2025, within the UK NEQAS Haematology program from Watford, United Kingdom, 120 CBC samples were analyzed, comprising a total of 480 parameters: white blood cells (WBC), red blood cells (RBC), hemoglobin (Hb), and platelet count (PLT). Also, 36 RBC component samples were analyzed for Hb and hematocrit (Hct), and 36 platelet component samples were analyzed for PLT. All samples were liquid human blood samples. Analyses were performed on HORIBA ABX Micros ES 60 hematology analyzer. The obtained results were compared by the organizer with those of other participants and presented as a Deviation Index (DI), which is identical to the Z-score. **Results:** Among the CBC parameters, 31 (6.5%) results were out of consensus and unacceptable: 8 (1.7%) WBC results and 23 (4.8%) PLT results. Among the blood component parameters, 3 platelet results (8.3%) were out of consensus but acceptable, while 1 hemoglobin result (2.7%) and 1 hematocrit result (2.7%) were out of consensus and unacceptable. **Conclusion:** A total of 449 (93.5%) CBC parameters and 31 (86.3%) blood component parameters were within consensus. The parameters most frequently out of consensus were platelet counts, particularly in samples with decreased platelet counts. Variability in out-of-consensus results was associated with sample delays, especially during the COVID-19 pandemic, which significantly affected platelet counting by the impedance method. Transport time, conditions, and temperature fluctuations influence results, particularly leukocyte and platelet counts, and these factors should be carefully considered both in external quality assessment programs and in routine sample handling.

Key words: external, quality, control, CBC, blood, components

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PRIMENA TESTOVA AGREGACIJE TROMBOCITA U PROCENI EFIKASNOSTI ANTITROMBOCITNE TERAPIJE

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UVOD Adekvatna blokada trombocitne funkcije primenom antitrombocitnih lekova ima ključnu ulogu u prevenciji i lečenju arterijskih tromboza i tromboembolijskih komplikacija.Efikasnost antitrombocitne terapije se utvrđuje testovima inhibiranosti trombocita.
CILJ RADA Uporediti efikasnost dvojne antiagregacione terapije u odnosu na monoterapiju procenom funkcije trombocita kod pacijenata Opšte bolnice u Somboru u 2025. godini
MATERIJALI METODE Retrospektivnom analizom podataka dobili smo uvid u broj odrađenih analiza na aparatu Multiplate (Roche).Na osnovu rezultata testiranja procenjivana je efikasnost antitrombocitne terapije.
REZULTATI RADA Retrospektivna studija je obuhvatila **236** pacijenta tokom 2025. godine.Od ukupnog broja ispitanika bilo je 133 (56,35%) osoba muškog pola i 103 (43,65%) ženskog pola.
Efikasnost antiagregacione terapije se procenjivala na osnovu cut off vrednosti ASPI i ADP- HS testa.Adekvatnim odgovorom na acetilsalicilnu kiselinu smatrala se vrednost u ASPI testu ispod 400 AU.Efikasna terapija tienopiridinima bila je pri vrednostima ADP-HS ispod 468 AU.
Dvojnu antiagregacionu terapiju u navedenom periodu primao je **71** pacijent (30%). Adekvatan efekat acetilsalicilne kiseline evidentiran je kod 51 pacijenta **(70,84%)**. Primena tienopiridina kod ovih pacijenata bila je efikasna u 49 slučajeva **(70,00 %)**. Adekvatan efekat oba leka je bio prisutan kod 50 pacijenata (70,42%). Kod 8 pacijenata (11,26%) izostao je efekat oba antiagregaciona leka..
Na mono antiagregacionoj terapiji evidentirano je **165** pacijenata (70%). Efekat acetilsalicilne kiseline je ispitivan kod 98 pacijenta (59,39%) . Adekvatan efekat postignut je kod 58 (**59,18**%) . Efekat tienopiridina je ispitivan kod 67 (40,60%) ispitanika.Odgovarajući efekat imalo je 37 **(55,22 %)** . Bazalna funkcija trombocita ispitivana je primenom TRAP testa.Fiziološka funkcija trombocita bila je prisutna kod 50 (83,10 %) ispitanika na dvojnoj antiagregacionoj terapiji, dok je suprafiziološka funkcija evidentirana kod 12 (16,90%) .Kod pacijenata na monoterapiji fiziološka funkcija trombocita bila je evidentirana kod 134 (81,20 %) pacijenata a suprafiziološka kod 31 (18,80%) pacijenta.
ZAKLJUČAK Nakon sprovedenog ispitivanja uočava se veća efiksnost dvojne antiagregacione terapije. Odgovor na primenjenu terapiju može izostati usled smanjene bioraspoloživosti leka i usled interakcije sa drugim lekovima.

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STRUKTURA DOBROVOLJNIH DAVALACA KRVI PRIJEDORSKE REGIJE PREMA ABO I RH KRVNIM GRUPAMA I POLU

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Uvod: Određivanje ABO i RhD krvne grupe predstavlja osnovni preduslov za bezbjednu primjenu krvi i krvnih komponenti. Poznavanje zastupljenosti krvnih grupa među dobrovoljnim davaocima krvi značajno je za planiranje zaliha krvi i obezbjeđivanje stabilnosti transfuzijskog sistema.
Cilj: Analiza strukture dobrovoljnih davalaca krvi prijedorske regije prema ABO i Rh krvnim grupama i polu.
Metode: Retrospektivno su analizirani podaci iz informacionog sistema Zavoda za transfuzijsku medicinu Republike Srpske za područje koje pokriva Služba za transfuzijsku medicinu Prijedor. U periodu od 1. januara 2010. do 31. decembra 2024. godine registrovano je 10.630 dobrovoljnih davalaca krvi.
Rezultati: Među registrovanim davaocima najzastupljenija je bila A pozitivna krvna grupa sa 3.311 (31,1%) davalaca, zatim O pozitivna sa 3.211 (30,2%). O negativna krvna grupa bila je zastupljena kod 846 (8,0%), A negativna kod 747 (7,0%), B pozitivna kod 1.437 (13,5%), B negativna kod 358 (3,4%), AB pozitivna kod 583 (5,5%), a AB negativna kod 137 (1,3%) davalaca. Od ukupnog broja registrovanih davalaca, 8.579 (80,7%) bili su muškarci, a 2.051 (19,3%) žene. Kod žena je najzastupljenija bila O pozitivna krvna grupa (31,4%), dok je kod muškaraca najzastupljenija bila A pozitivna krvna grupa (31,6%).
Zaključak: Struktura ABO i Rh krvnih grupa među dobrovoljnim davaocima krvi prijedorske regije pokazuje visok stepen podudarnosti sa podacima iz zemalja regiona i Evrope. Najzastupljenije krvne grupe su A pozitivna i O pozitivna. Muškarci čine dominantan udio u ukupnom broju registrovanih davalaca krvi, što ukazuje na potrebu za dodatnim aktivnostima usmjerenim na povećanje učešća žena u dobrovoljnom davalaštvu krvi.
Ključne riječi: dobrovoljni davalac krvi, ABO sistem, RhD sistem, krvna grupa, pol.

PP 047

STRUCTURE OF VOLUNTARY BLOOD DONORS IN THE PRIJEDOR REGION ACCORDING TO ABO AND RH BLOOD GROUPS AND MALE AND FEMALE DISTRIBUTION

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Introduction: Determination of ABO and RhD blood groups is a fundamental prerequisite for the safe use of blood and blood components. Knowledge of the distribution of blood groups among voluntary blood donors is essential for planning blood supplies and ensuring the stability of the transfusion system.
Objective: To analyze the structure of voluntary blood donors in the Prijedor region according to ABO and Rh blood groups and male and female distribution.
Methods: Data from the information system of the Institute of Transfusion Medicine of the Republic of Srpska were retrospectively analyzed for the area covered by the Prijedor Transfusion Medicine Service. Between January 1, 2010, and December 31, 2024, a total of 10,630 voluntary blood donors were registered.
Results: Among the registered donors, the most common blood group was A positive, accounting for 3,311 (31.1%) donors, followed by O positive with 3,211 (30.2%) donors. O negative blood group was present in 846 (8.0%), A negative in 747 (7.0%), B positive in 1,437 (13.5%), B negative in 358 (3.4%), AB positive in 583 (5.5%), and AB negative in 137 (1.3%) donors. Of the total number of registered donors, 8,579 (80.7%) were male and 2,051 (19.3%) were female. Among female donors, the most prevalent blood group was O positive (31.4%), whereas among male donors, A positive was the most prevalent blood group (31.6%).
Conclusion: The distribution of ABO and Rh blood groups among voluntary blood donors in the Prijedor region shows a high degree of similarity to data reported from neighboring countries and Europe. The most prevalent blood groups are A positive and O positive. Male donors constitute the majority of registered blood donors, indicating the need for additional activities aimed at increasing the participation of female donors in voluntary blood donation.
Keywords: voluntary blood donor, ABO system, RhD system, blood group, male, female.

PP 048

BANKA MATIČNIH ĆELIJA HEMATOPOEZE KAO ZNAČAJAN SEGMENT TRANSFUZIJSKE DELATNOSTI

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Uvod: Razvoj transplantacione medicine i savremenih metoda lečenja nametnuo je potrebu za organizovanim prikupljanjem, obradom, kriokonzervacijom i skladištenjem matičnih ćelija. U cilju unapređenja transplantacionog programa u Vojvodini, u Zavodu za transfuziju krvi Vojvodine je 2014. godine formirana Banka matičnih ćelija hematopoeze, u kojoj se vrši obrada, kriokonzervacija i dugoročno skladištenje matičnih ćelija bolesnika lečenih na Klinici za hematologiju Univerzitetskog kliničkog centra Vojvodine.
Cilj rada: Prikazati značaj Banke matičnih ćelija hematopoeze kao segmenta transfuzijske delatnosti i njen doprinos uspešnom sprovođenju autologne transplantacije u lečenju hematoloških bolesnika.
Materijal i metod rada: Prikaz organizacije rada Banke matičnih ćelija hematopoeze, kao i postupaka prikupljanja, transporta, obrade, kriokonzervacije, dugoročnog skladištenja i kontrole kvaliteta matičnih ćelija.
Rezultati: Od osnivanja Banke do danas uspešno je izvršeno 190 postupaka kriokonzervacije matičnih ćelija hematopoeze za autolognu transplantaciju. U zavisnosti od prinosa matičnih ćelija, odnosno broja CD34+ ćelija, za jednog bolesnika pripremljena su dva ili više kriokonzervisanih preparata. Primenom standardizovanih procedura, sistema kvaliteta i kontinuirane kontrole procesa obezbeđeni su uslovi za bezbedno čuvanje, sledljivost i blagovremenu dostupnost transplantata u trenutku lečenja bolesnika.
Zaključak: Banka matičnih ćelija hematopoeze predstavlja značajan segment savremene transfuzijske delatnosti i važnu podršku transplantacionom programu. Njeno funkcionisanje omogućava blagovremenu dostupnost kvalitetnih autolognih transplantata, unapređuje ishod lečenja bolesnika i doprinosi daljem razvoju transplantacione medicine u Republici Srbiji.
Ključne reči: matične ćelije hematopoeze, kriokonzervacija, autologna transplantacija, transfuzijska delatnost.

PP 048

HEMATOPOIETIC STEM CELL BANK AS A SIGNIFICANT SEGMENT OF TRANSFUSION ACTIVITY

Introduction: The development of transplantation medicine and modern treatment modalities has created the need for organized collection, processing, cryoconservation, and storage of stem cells. In order to improve the transplantation program in Vojvodina, the Institute for Transfusion of Blood of Vojvodina established the Hematopoietic Stem Cell Bank in 2014. Within this unit, processing, cryoconservation, and long-term storage of stem cells from patients treated at the Hematology Clinic of the University Clinical Center of Vojvodina are performed.
Objective: To present the significance of the Hematopoietic Stem Cell Bank as a segment of transfusion activity and its contribution to the successful implementation of autologous transplantation in the treatment of hematological patients.
Material and Methods: A description of the organizational structure of the Hematopoietic Stem Cell Bank was provided, including procedures for collection, transport, processing, cryoconservation, long-term storage, and quality control of stem cell products.
Results: Since the establishment of the Bank, 190 cryopreservation procedures of hematopoietic stem cells for autologous transplantation have been successfully performed. Depending on the stem cell yield, i.e., the number of CD34+ cells, two or more cryoconserved products have been prepared for a single patient. The application of standardized procedures, quality management systems, and continuous process monitoring has ensured safe storage conditions, traceability, and timely availability of grafts at the moment of patient treatment.
Conclusion: The Hematopoietic Stem Cell Bank represents a significant segment of modern transfusion activity and an important support to the transplantation program. Its functioning enables timely availability of high-quality autologous grafts, improves treatment outcomes in hematological patients, and contributes to the further development of transplantation medicine in the Republic of Serbia.
Keywords: hematopoietic stem cells, cryoconservation, autologous transplantation, transfusion activity.

PP 049

SEROLOŠKI I MOLEKULARNI SKRINING DAVAOCA KRVI NA MARKERE TRANSMISIVNIH BOLESTI ZAVODA ZA TRANSFUZIJU KRVI NIŠ U 2025 GOD

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Uvod:Zavod za transfuziju krvi Niš predstavlja vitalni deo zdravstvenog sistema čija je osnovna misija obezbedjenje dovoljnih količina bezbedne krvi i produkata od krvi.
Cilj rada:Statistička analiza je obuhvatila ukupan broj dobrovoljnih davalaca koji su u 2025 god.dali krv na podrucju rada Zavoda za transfuziju krvi Niš.
Metod:Svi uzorci su primarno testirani na automatizovanim sistemima Abbott Alinity,Ortho Vitros 3600,Siemens Centauer,Biorad Evolis primenom hemiluminiscentnih tehnika i Elisa testova za detekciju obaveznih markera (HbsAg,anti HCV at,HIV ag/ab, anti TP).Uzorci koji su pokazali inicijalnu reaktivnost su ponovo testirani u duplikatu sa istim protokolom,a u skladu sa standardnim operativnim procedurama ZTK Niš.
Rezultati:Tokom 2025 godine uzorci 47922 davalaca krvi testirani su na markere transfuzijom prenosivih bolesti.Nakon završenog protokola testiranja,ponovna serološka reaktivnost potvrdjena je kod 24 uzoraka na Hbs Ag,35 na anti HCV at,53 na HIV ag/ab,i 33 na anti TP.Status ponovljene sive zone zadržala su 2 uzorka na HbsAg,12 na anti HCV at,20 na HIV ag/ab i 15 na anti TP.Sto se tiče molekularnog testiranja bilo je NAT HBV 13,NAT HCV 3,NAT HIV -4 pozitivnih uzoraka.
Zaključak:Bezbedna krv je rezultat sinergije rigorozne selekcije davalaca i najsavremenijih metoda laboratorijskog testiranja.Uvodjenje obaveznog NAT testiranja dobrovoljnih davalaca krvi na prisustvo HBV,HCV,i HIV ifekcije značajno je povećalo bezbednost transfuzije krvnih produkata.

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ULOGA INSTAGRAMA U PROMOCIJI DOBROVOLJNOG DAVANJA KRVI NA PRIMERU KAMPANJE „NIŠTA BEZ ŽENA"

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Društvene mreže predstavljaju značajan kanal savremene komunikacije. Institut za transfuziju krvi Srbije (ITKS) redovno plasira promotivne kampanje putem Facebook-a, Instagram-a i Viber zajednice. Od 2025. objave na Instagramu bustovane su radi bolje vidljivosti široj populaciji. Kampanje („Jedan potez za život", „Kada život čeka ti odlučuješ", „Izvuci AS iz rukava", „Crveno je uvek IN") ostvarile su milionske preglede na mesečnom nivou. Više od 85% korisnika koji su pregledali sadržaj nisu direktni pratioci profila.
Cilj rada je analiza uticaja Instagram kampanje „Ništa bez žena" na vidljivost promotivnih aktivnosti i odziv žena dobrovoljnih davalaca krvi.
Izvršena je komparativna analiza rezultata kampanje „Ništa bez žena" 2025. i 2026. Promotivna kampanja 2025. bila je usmerena ka celokupnoj javnosti, a 2026. ciljano usmerena ka ženskoj populaciji iz Beograda starosti od 18 do 50 godina. Analizirani su podaci o broju pregleda kampanje, kao i odziv na akcije, posebno ženske populacije.
Broj pregleda Instagram kampanje „Ništa bez žena" porastao je sa 145 831 u 2025. na 623 072 u 2026. U akciji 2025. odazvale su se 153 osobe, od čega 98 žena, dok je krv dalo 129 osoba, među kojima 85 žena (65.9%). U 2026. akciji se odazvalo 210 osoba, od čega 168 žena, a krv je dala 181 osoba, uključujući 141 ženu (77.9%).
Instagram kampanje omogućavaju brzo širenje informacija, veliku vidljivost i efikasan su vid promocije koji motiviše građane da dobrovoljno daju krv. Kampanja „Ništa bez žena" pokazala je da ciljane aktivnosti uz adekvatno targetiranje populacionih grupa na društvenim mrežama mogu doprineti većem odzivu davalaca krvi.
KLJUČNE REČI: Instagram, dobrovoljno davalaštvo krvi, društvene mreže

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KAMPANJA DOBROVOLJNOG DAVANJA KRVI SA MIXED REALITY NAOČARIMA

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Institut za transfuziju krvi Srbije (ITKS) kontinuirano sprovodi promotivne aktivnosti radi povećanja broja dobrovoljnih davalaca krv. Od 4. do 15. avgusta 2025. u sali ITKS realizovana je kampanja "Davanje krvi sada postaje nesvakidašnje iskustvo", zasnovana na primeni Mixed Reality (MR) naočara.
Cilj rada je prikaz efikasnosti primene MR naočara u promociji dobrovoljnog davalaštva i procena njihovog uticaja na odziv davalaca.
Priprema kampanje obuhvatila je edukaciju zaposlenih, izradu ankete za davaoce, dizajn promotivnih i video materijala, kao i medijsku promociju. Davaoci su birali između dva virtuelna okruženja (Zen Garden i Intergalactic). Sprovedena je kvalitativna analiza uvedene inovacije i analiza anketa popunjenih nakon donacije, radi poređenja iskustva sa i bez primene MR naočara. Izvršena je i komparativna analiza broja prikupljenih jedinica krvi u sali ITKS u istom periodu 2024. i 2025.
Tokom kampanje prikupljena je 1 241 jedinica krvi, što predstavlja povećanje od 10.5% u odnosu na isti period 2024. MR naočare koristilo je 395 davalaca (31.8%), dok je prvi put krv dala 301 osoba, 21.9% više nego prethodne godine. Prosečna starost davalaca koji su koristili MR naočare iznosila je 36.4 godine. U anketi 76.6% davalaca ocenilo je da je davanje krvi prijatnije uz MR tehnologiju, 81.2% davalaca ponovilo bi ovo iskustvo, a 89.3% preporučilo bi ih prijateljima. Mediji su svakodnevno izveštavali o MR tehnologiji u dobrovoljnom davalaštvu.
Upotreba digitalnih tehnologija predstavlja inovativan i efikasan pristup u promociji dobrovoljnog davalaštva. Integracija virtuelnih sadržaja povećala je motivisanost za dobrovoljno davanje. Rezultati ukazuju na potencijal šire primene sličnih tehnoloških rešenja u budućim kampanjama.
KLJUČNE REČI: inovacije, tehnologija, motivacija

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ISKUSTVA U PRIMENI DTT METODE KOD PACIJENATA NA TERAPIJI ANTI-CD38 ANTITELIMA

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Uvod: Terapija multiplog mijeloma monoklonskim anti-CD38 antitelima, može dovesti do smetnji u pretransfuzionim testiranjima. Vezivanje anti-CD38 antitela za antigen CD38 na membrani eritrocita, dovodi do panaglutinacije i može maskirati prisustvo klinički značajnih antitela. Ditiotreitol (DTT) razara disulfidne veze CD38 antigena na eritrocitima i omogućava pouzdaniju interpretaciju seroloških reakcija.
Cilj: Prikazati iskustvo laboratorije kroz tehnički aspekt primene DTT metode, u rešavanju smetnji u pretransfuzionim testiranjima.
Materijal i metode: Kod pacijenata lečenih terapijom anti-CD38 antitelima, sa pozitivnim indirektnim *Coombs*-ovim testom (IAT), primenjena je „in house" DTT metoda. Komercijalni test eritrociti za skrining anti-eritrocitnih antitela tretirani su DTT-om u odnosu 1:4 i inkubirani 30–45 minuta na 37˚C, u skladu sa preporukama AABB *Techical Manual*. Nakon tretmana test eritrocita DTT-om, ponovljeno je pretransfuziono testiranje, a rezultati su upoređeni sa testiranjem sa netretiranim eritrocitima.
Rezultati: Kod analiziranih uzoraka pacijenata pre primene DTT uočene su izražene smetnje u pretransfuzionom testiranju u IAT i intereakciji u vidu panaglutinacije koja je onemogućavala pouzdanu identifikaciju aloantitela. Nakon tretiranja eritrocita DTT metodom zabeležen je nestanak specifične reaktivnosti u IAT. Time je omogućena jasna interpretacija seroloških rezultata i nastavak pretransfuzionog testiranja, uključujući i izbor odgovarajuće kompatibilne jedinice eritrocita za transfuziju.
Zaključak: Na osnovu iskustva naše laboratorije, primena DTT metode omogućila je uspešno rešavanje interferencije izazvane monoklonskom anti-CD38 terapijom, odnosno isključivanje prisustva klinički značajnih aloantitela.
Ključne reči:Anti-CD 38 antitela, Ditiotreitol (DTT), multipli mijelom

PP 052

LABORATORY EXPERIANCE WITH THE DTT METHOD IN PATIENTS RECEIVING ANTI-CD38 THERAPY

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Introduction: Treatment of multiple myeloma with anti-CD38 monoclonal antibodies may interfere with pretransfusion testing. Binding of anti-CD38 antibodies to the CD38 antigen in red blood cells causes panagglutination and may mask the presence of clinically significant alloantibodies. Dithiothreitol (DTT) disrupts the disulfide bonds of the CD38 antigen on erytrocites, enabling reliable interpretation of serological reactions.
Aim: To present our laboratory experiance with the technical application of the DTT method in resolving interference during pretransfusion testing.
Materials and Methods: An in-house DTT method was applied in patients receiving anti-CD38 therapy who had positive indirect antiglobulin tests (IAT). Commercial reagent red blood cells for antibody screening were treated with DTT at 1:4 ratio and incubated for 30-45 minutes at 37˚C, according to the recommendations of the **AABB Technical Manual.** Following DTT treatment, pretransfusion testing was repeated, and the results were compared with those obtained using untreated red blood cells.
Results: Before DTT treatment, all analyzed patients samples showed panagglutinaton in IAT, masking the presence of alloantibodies. After DTT treatment, the nonspecific reactivity in the IAT was eliminated. This enabled clear interpretation of serological findings and selection of compatible red blood cell units for transfusion.
Conclusion: Based on our laboratory experiance, the DTT method successfully resolved serological interference caused by anti-CD38 monoclonal antibodies, enabling the reliably exclusion of clinically significant alloantibodies.
Key words: Anti-CD 38 antibodies, Dithiothreitol (DTT), multiple myeloma

PP 053

UNAPREĐENJE BEZBEDNOSTI KRVI U TRNSFUZIJSKOJ MEDICINI KROZ ANALIZU GREŠAKA U PRAKSI

Suzana Kačar
Zavod za transfuziju krvi Niš

Uvod: Bezbednost transfuzije podrazumeva kontrolu i praćenje svih aktivnosti u transfuzijskom lancu kroz selekcije i prikupljanja krvi od davoca, preko njene obrade pa sve do primene krvnih komponenti kod pacijenata. Pored sistema za upravljanje kvalitetom značajnu ulogu ima hemovigilanca odnosno organizovano praćenje ozbiljnih neželjenih događaja povezanih sa davanjem ili primanjem krvi.
Ovakav pristup omogućava prepoznavanje kritičnih tačaka u procesu i doprinosi unapređenju transfuzijske prakse.
CILJ RADA: Cilj istraživanja bio je da se identifikuju, prikažu i analiziraju neželjeni i neočekivani događaji u transfuzijskoj praksi koji mogu predstavljati rizik za davaoce krvi i pacijente.
METOD RADA: Sprovedena je retrospektivna analiza u trajanju od dve godine. U istraživanju su uključene sve prijavljene greške koje su evidentirane, obrađene i analizirane u Zavodu za transfuziju krvi Niš.
REZULTATI: Utvđene greške razvrstane su prema vrsti, učestalosti i fazi procesa u kome su nastale. Za svaki zabeležen propust analizirani su mogući uzroci kao i mere koje bi mogle doprineti njihovom sprečavanju. Rezultati su pokazali da nijedna od registrovanih grešaka nije dovela do posledica po davaoca ili primaoca.
Najveći broj grešaka zabeležen je u preanalitičkoj fazi procesa, pri čemu je ljudski faktor najčešći uzrok njihovog nastanka.
ZAKLjUČAK: Sistem prijavljivanja i analize grešaka predstavlja važan mehanizam za unapređenje kvaliteta rada i smanjenje rizika od neženjenih događaja u transfuzijskoj medicini. I ako se pojedinačne transfuzijske greške ne mogu u potpunosti eliminisati, njihov broj i posledice mogu se značajno smanjiti sistematskim pristupom.

PP 053

PP 054

ASSESSMENT OF THE PROFESSIONAL SKILLS OF NURSES IN PERFORMING ACTIVITIES RELATED TO BLOOD DONATION

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Abstract: Activities related to blood donation require nurses to combine professional knowledge, practical skills, communicative competence, and a high degree of responsibility. In transfusion practice, nurses are actively involved in ensuring donor safety, the proper performance of procedures, adherence to ethical principles, and maintaining trust in the system of voluntary and non-remunerated blood donation.
Aim: To assess the level of professional skills of nurses in performing activities related to blood donation, and to identify the main difficulties and needs for additional training in transfusion practice.
Materials and Methods:A direct, individual, and anonymous questionnaire survey was conducted among 59 nurses working in structures of the National Transfusion System. The study included professionals from three transfusion hematology centres and eight transfusion hematology departments in the cities of Sofia, Burgas, Pleven, Sliven, Kyustendil, Vratsa, Lom, and Vidin. Documentary, sociological, and statistical methods were applied for data collection and analysis. The data were processed using IBM SPSS Statistics 20.0, and the graphical presentation of the results was performed with Microsoft Excel.
Results: All surveyed nurses were women, with 66.10% being over 50 years of age. A more pronounced tendency towards ageing of the nursing staff was observed in transfusion hematology departments compared with transfusion hematology centres. Respondents gave the highest self-assessments for their teamwork skills — 86.44%, knowledge of ethical principles — 77.97%, and venipuncture skills in blood collection — 72.88%. Knowledge of the effects of blood donation on the body and the possible risks was reported by 62.71% of respondents. Lower values were recorded for awareness of the regulatory framework in the field of transfusion hematology — 49.15%, as well as for communication skills with anxious or difficult donors — 54.24%. The leading difficulties when entering practice were identified as the high level of professional responsibility and fear of making mistakes — 67.80%, as well as stress when working with blood donors — 59.32%. The most preferred forms of continuing professional development were in-house hospital training — 67.80%, and short-term courses — 59.32%.
Conclusion: The results show that nurses possess well-developed practical, ethical, and teamwork skills in activities related to blood donation. At the same time, the findings reveal a need to further develop knowledge of the regulatory framework, communication with different groups of blood donors, stress management, and prevention of professional errors. Targeted continuing education would contribute to increasing professional confidence, improving the quality of nursing care, and enhancing safety in transfusion practice.
Keywords: nurses, professional skills, blood donation, transfusion practice, training, safety.

PP 054

PP 055

PRIKAZ PODATAKA IZ NACIONALNOG REGISTRA UROĐENIH KOAGULOPATIJA

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Uvod. Nacionalni Registar urođenih koagulopatija se od osnivanja 1963. godine nalazi u Institutu za transfuziju krvi Srbije i predstavlja centralnu bazu podataka o pacijentima sa hemofiljom, von Willebrandovim oboljenjem i retkim koagulopatijama. **Cilj.** Prikazati aktuelne podatke o pacijentima i preparatima za lečenje. **Materijal i metode** Analizirali smo aktuelne podatake iz Nacionalnog Registra. **Rezultati:** U Srbiji je do decembra 2025. godine registrovano 1064 pacijenata sa urođenim koagulopatijama - 493 pacijenta sa hemofilijom A (HA) , 98 sa hemofilijom B (HB), 357 sa von Willebrand-ovim oboljenjem (VWB) i 116 sa retkim koagulopatijama (RK). Težak oblik HA je prisutan kod 195 (39,6%), umeren oblik kod 46 (9,3%) i blag oblik kod 252 (51,1%) pacijenata. Među 98 pacijenata sa HB 31 (31,6%) ima težak oblik, 16 (16,3%) je sa umerenim i 51 (52,1 %) sa blagim oblikom oboljenja. Inhibitori su prisutni kod 15 pacijenta sa HA. Od 357 (143 muškaraca i 214 žena) pacijenata sa VWB, 21 (5,9%) ima težak oblik, 96 (26,9%), umeren oblik i 240 (67,2%) blag oblik oboljenja. Od 114 pacijenata sa retkim koagulopatijama težak oblik ima 20 pacijenata - 2 pacijenta sa afibrinogenemijom, 2 sa kombinovanim deficitom FV+FVIII, 10 sa deficitom FVII i 6 sa deficitom FXIII. Lečenje pacijenata se sprovodi u 9 tercijarnih centara - na klinikama za hematologiju i pedijatriju u Beogradu, Novom Sadu, Nišu i Kragujevcu i 30 sekundarnih zdravstvenih centara. Svih 226 (100%) pacijenata sa teškim oblicima HA i HB nalaze se na redovnoj profilaksi, kao i 10/21 (47%) pacijenata sa teškim oblikom VWB. Pacijenti sa teškim oblicima retkih koagulopatija su na redovnoj profilaksi u skladu sa kliničkom procenom lekara. Potrošnja koncentrata FVIII u 2024. je dostigla 3,4 IJ/stanovniku, koncentrata, a FIX 1.10 IJ/stanovniku . Ovo je višestruko povećanje u odnosu na 2000-tu godinu (0,27 IJ/stanovniku za koncentrat FVIII i 0,03 IJ/stanovniku za koncentrat FIX). Od 2020. je registrovan emicizumab koji se primenjuje kod 85 pacijenata sa HA i 13 pacijenata sa HA sa inhibitorima.
Zaključak. Nacionalni registar urođenih koagulopatija predstavlja značajan instrument za planiranje i unapređenje zdravstvene zaštite pacijenata preko kontinuirane saradnje udruženja pacijenata sa hemofilijom, zdravstvenih i nadležnih državnih institucija.

Ključne reči: hemofilija, von Willebrand, retke, koagulopatije, registar

PP 055

OVERVIEW OF DATA FROM THE NATIONAL REGISTRY OF INHERITED COAGULATION DISORDERS

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Introduction. Since its establishment in 1963, the National Registry of Inherited Coagulation Disorders has been located at the National Blood Transfusion Institute of Serbia and represents the central database of patients with hemophilia, von Willebrand disease, and rare coagulation disorders.**Aim**. To present current data on patients and treatment products.**Material and Methods.** Current data from the National Registry were analyzed.**Results.** By December 2025, a total of 1,064 patients with inherited coagulation disorders had been registered in Serbia: 493 patients with hemophilia A (HA), 98 with hemophilia B (HB), 357 with von Willebrand disease (VWD), and 116 with rare bleeding disorders (RBDs). Severe HA was present in 195 (39.6%) patients, moderate HA in 46 (9.3%), and mild HA in 252 (51.1%) patients. Among 98 patients with HB, 31 (31.6%) had severe disease, 16 (16.3%) moderate disease, and 51 (52.1%) mild disease. Inhibitors were present in 15 patients with HA. Among 357 patients with VWD (143 males and 214 females), 21 (5.9%) had severe disease, 96 (26.9%) moderate disease, and 240 (67.2%) mild disease. Of 116 patients with rare coagulation disorders, 20 had severe forms: 2 with afibrinogenemia, 2 with combined FV+FVIII deficiency, 10 with FVII deficiency, and 6 with FXIII deficiency. Treatment is provided in 9 tertiary care centers, at hematology and pediatric clinics in Belgrade, Novi Sad, Nis, and Kragujevac, as well as in 30 secondary healthcare centers. All patients with severe HA and HB are on regular prophylaxis, as are 10/21 (47%) patients with severe VWD. Patients with severe forms of rare coagulation disorders receive regular prophylaxis according to the physician's clinical assessment. Consumption of FVIII concentrates in 2024 reached 3.4 IU per capita, while FIX concentrate consumption reached 1.10 IU per capita, representing a marked increase compared with the year 2000 (0.27 IU per capita for FVIII concentrate and 0.03 IU per capita for FIX concentrate). Since 2020, emicizumab has been registered and is currently used in 85 patients with HA and 13 patients with HA with inhibitors. **Conclusion.** The National Registry of Inherited Coagulation Disorders represents an important instrument for planning and improving healthcare for patients through continuous cooperation between hemophilia patients association, healthcare institutions and relevant governmental authorities.
Key words: haemophilia, von Willebrand, rare, bleeding, disorders, registry

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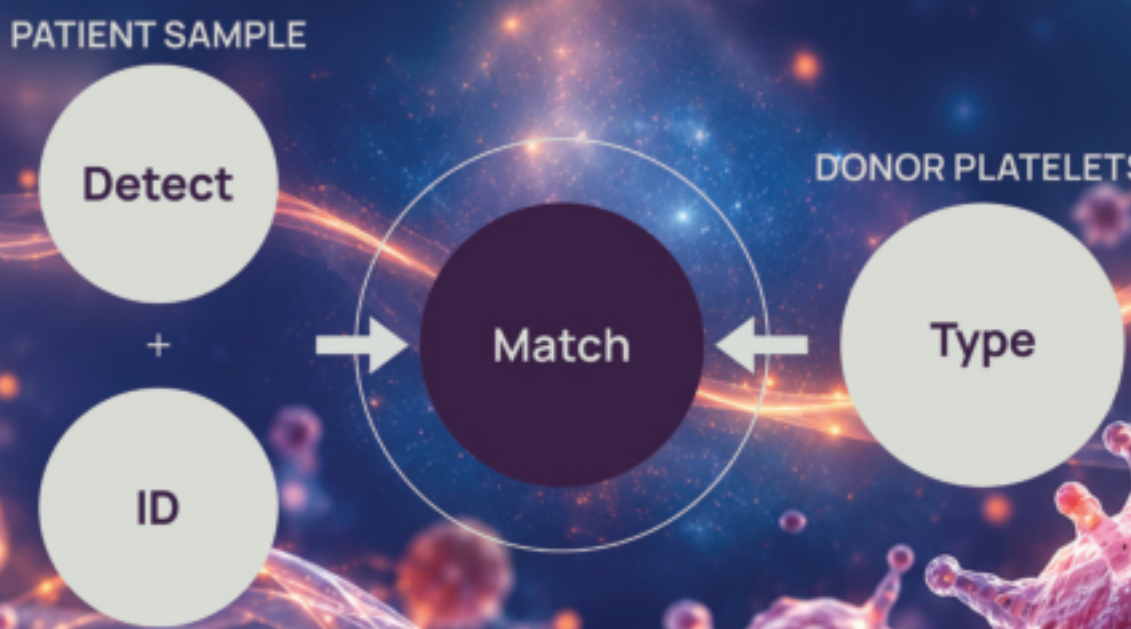
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